# The Journal of the American Medical Association

**Published Under the Auspices of the Board of Trustees**

VOL. 135, NO. 8 — CHICAGO, ILLINOIS — OCTOBER 25, 1947

COPYRIGHT, 1947, BY AMERICAN MEDICAL ASSOCIATION

## THE FUTURE OF OTOLARYNGOLOGY

**Chairman's Address**

JOHN MACKENZIE BROWN, M.D.
Los Angeles

It is difficult to create a prophetic analysis on any subject, particularly in the field of medical science. The most accurate predictions have usually been made on the basis of a careful study of history. The past tells one what to expect of the future. Because the history of otolaryngology has been highlighted by so many important discoveries and contributions to the welfare of the human race, it is impossible for me to approach the future of this specialty with other than optimism.

Otolaryngology in the future will become a specialty not only of surgical but also of medical practice, which should attract the ablest men in the profession. There are numerous reasons for this view. The otolaryngologist of the future will find that he is the master of a great field of scientific thought and inquiry as well as of practical medicine and surgery. The very nature of the anatomic region assigned to him is enough excuse for the preceding statement. The changes in the specialty are indeed profound and will become more so as time goes on. Those who are living in this age are fortunate to be able to see this transition—a change which is bound to be only for the best. The otolaryngologist must release himself from the bonds of conservative restraint as far as the manner of scientific thinking is concerned. He must realize that the changes in this specialty are truly blessings.

In the field of otology several years ago the physician was primarily concerned with the surgical search for infection. Otitis media, mastoiditis and its numerous complications were the compelling interests. The otologist knew that the temporal bone housed a most intricate and complicated organ, which served the function of hearing and equilibrium, but in only rare instances did he turn an analytic view toward this field. He was quite pessimistic about the subject of hearing and hearing deficiencies; he was convinced that little could be done for his patients and in view of the other pressures from septic processes was willing to forget temporarily the functional aspect of otology. Consequently, when chemotherapy and biotherapy came on the scene and drastically reduced the necessity for surgical intervention in disease of the temporal bone, many otologists found themselves at a loss temporarily, and some viewed with alarm the changing nature of the specialty. It was considered by many that there were no new horizons to be sought and that the otology of the past was a thing of glorious memory. On the contrary, it was this same blessing of chemotherapy and biotherapy which removed much of the work entailed by the search for infection and which in turn made it possible for the specialist of today and tomorrow to take an entirely new slant on the problem of disease of the temporal bone. Now that the surgical complications of the acute form of otitis media and mastoiditis have become relatively uncommon the otologist may expect to see chronic suppuration less frequently in the future; he can look forward to a period when he can turn his thoughts to the functional aspects of the ear.

That this new approach is well under way may be ascertained by the present day status of fenestration surgery. The renewed interest in vestibular diseases, including Ménière's disease, the vast and pressing clinical problem of the causation of tinnitus and the innumerable problems suddenly posed by the aviation age have resulted in an entirely new and vital interest in the functional aspects of the ear. Deafness due to otosclerosis may now be viewed with far less pessimism than was necessary in the past. Regardless of the controversial nature of fenestration surgery, it is safe to say that the procedure of fenestration of the labyrinth is a surgical approach which is here to stay. No doubt this approach will undergo modifications in the future, but the fact remains that deaf people are hearing today as the result of fenestrations of their labyrinths. It is also a fact that patients who suffered the dizziness, tinnitus and deafness of Ménière's disease have in numerous instances been greatly improved and even cured by the surgical approach to the labyrinth employed by Day and Cawthorne. One cannot overestimate the valuable work in aural rehabilitation which has been contributed by the otologic services of the various military branches of the government following World War II. The utilization of radium in the nasopharynx, with excellent results in conduction deafness and tubal obstruction, was hastened by military usage. The newer approach to the use of hearing aids and the reeducation by acoustic training of deafened adults as well as children certainly come as a distinct credit to the members of the profession. The educational treatment of the deafened child, utilizing modern pedagogic, psychologic and acoustic technics and beginning as early as possible, even at the age of 2 years, will call for the increased cooperation and support of the otologist. He finds himself daily subjected to innumerable questions from the aviation industry. Men are being catapulted into altitudes and subjected to changes in atmospheric pressure for which the human organism was not designed. The otologist must answer these questions and must know how to prevent as well

Read before the Section on Laryngology, Otology and Rhinology at the Ninety-Sixth Annual Session of the American Medical Association, Atlantic City, N. J., June 12, 1947.

as treat the new types of ear diseases produced by the air age. The acoustic trauma of war is at least equalled if not surpassed by the acoustic trauma of industry today. The aero otitis media of the conventional airplane will become an infinitely greater problem in jet-propelled aircraft. The vestibular changes incident to rapid air and subsurface travel certainly will tax the ingenuity and the knowledge of the otologist. One can only be challenged by the field of otology today; as long as there are unanswered questions in any field of scientific thought, that particular field is bound to grow. One can see the analogy in physics. The unanswered questions of the atom proved to be the motivation which finally resulted in the unlocking of atomic power.

It is true that the approach to rhinologic disease has undergone even more radical changes than has otologic practice. Rhinologists of twenty-five years ago were bent on a search for pus and infected mucosa; then eradication was the main emphasis in rhinologic practice. Today, while obstructions and pus are still present, the nose and its adnexa are now studied in the light of physiologic and chemical changes. New interpretations of allergy and bacteriology, as well as of nasal physiology, almost completely reverse the practices of the rhinologists of twenty-five years ago. The rhinologist must now broaden his own horizons to include intensive study and interest in these contributing fields. Allergy has its constant manifestations in the nose and paranasal sinuses. Proper consideration of primary allergy as well as of the frequently associated secondary infections is essential to the rhinologist. It is true that he must become much more of an internist, but at the same time he must not think that surgical rhinology is a thing of the past. Pus and obstructions are still problems. The importance of the nose in the physiologic mechanism of respiration is now more fully understood and has become an integral part of present day rhinologic practice. The rhinologist of tomorrow will find himself in a position in which he must practice reconstructive surgery of the nasal pyramid as well as of the internal nose and sinuses in order to restore normal nasal function to his patients. His surgical field has not contracted; it has greatly expanded.

The sphere of laryngology and bronchoesophagology has become a necessary part of the daily practice of every otolaryngologist. There will always be foreign bodies in the food and air passages. Unfortunately, malignant conditions in these areas are on the increase rather than on the decrease. Improvements and advances in thoracic surgery have necessitated greater cooperation between the thoracic surgeon and the laryngologist. Accordingly this particular branch has become so highly specialized and has such a constantly expanding future that some physicians have been forced to restrict their practice to this field alone.

Not only have the changes in this specialty been generated through the efforts of the otolaryngologist, but innumerable aspects of change have come from contemporaries and colleagues in other fields of endeavor. He cannot forget the brilliant contributions of his pharmacologic colleagues in the development of the sulfonamide drugs, penicillin, streptomycin and the new antihistaminic drugs, "pyribenzamine" and "benadryl." Also homage must be paid to those colleagues in physics, physiology and psychology who have contributed so much to the knowledge of the acoustic end organ. The outstanding work in acoustic physics and acoustic physiology has provided a new insight into the function of the cochlea, of the middle ear and of the vestibular apparatus. One can look forward undoubtedly also to utilization of new radioactive weapons in his practice. Radium and deep roentgen therapy are well known to all. Undoubtedly the technic of applying other radioactive materials will be developed in the near future. The use of nitrogen mustards, the administration of various isotopes and the ultimate use of the cyclotron against disease may become a part of medical practice. We are at the threshold of a new and in many ways different era in otolaryngologic theory and practice. However, at this point it is important to emphasize that in spite of all the preceding statements and in spite of all the knowledge of constant change, it must not be forgotten that certain diseases will probably always exist and, even more important, that certain fundamental considerations in surgical practice as well as in diagnosis will remain the same. Sound otolaryngologic practice will always be based on anatomic, physiologic and pathologic facts. The otolaryngologist of tomorrow, just as he is today, will have to be an outstanding clinical anatomist and pathologist. The present state of efficiency in this specialty is due to the wonderful work and foresight of the American Board, with the active support and cooperation of medical schools and hospitals. The Board cannot receive too much praise for the time and energy spent on this important educational project. I wish to add my personal thanks for the many hours spent by every member of the Board on behalf of this specialty.

In order to educate the otolaryngologist of the future to be one of the most skilled practitioners in medicine, it is necessary to plan for a long period of sound basic training as well as of practical experience. Undoubtedly such a man will not only be required to possess good knowledge of medicine and surgery but will have to be adept in the meticulous technics of otologic surgery and bronchoesophagologic procedures. He will have to possess a sound knowledge of acoustic physics in order to treat properly his otologic patients. He will have to be an excellent allergist and immunologist in order to do proper justice to his rhinologic patients. He will have to master certain fundamental technics in plastic reconstructive surgery in order adequately to treat deformities of the nose. And last but far from least he must be a fine practitioner of psychosomatic medicine, so that he may properly evaluate the problems of his patients.

Now that the course of study in otolaryngology has been extended to three years, including one year of basic sciences, the problem arises as to the best method of training residents. There are two chief methods to consider. First, the student may take a nine months' academic course either at the University of Pennsylvania or Washington University or in some similar institution. This should be followed by twenty-four months in an accepted hospital or hospitals. I say hospitals because I can see how a student could take his residency to great advantage both to himself and to the hospitals by spending one year in a children's hospital and one year in a general hospital. Some hospitals are being classified by the American Medical Association as offering limited residencies. These hospitals with limited residency facilities must be adequately staffed and have sufficient beds and outpatients for proper training. The hospitals should have an adequate library and well equipped clinical laboratories. I am sure that in this country there are many such hospitals, which could be organized and set up for

worthwhile residencies in otolaryngology on a limited basis. Such a move would do a great deal not only for the hospital, attending staff members and residents but especially for the welfare of the patients; and it would increase the number of otolaryngologists in training now badly needed. The other method of training is by a residency in a hospital that is equipped to give its own basic science courses or is in close proximity to a medical school where the proper facilities and teachers are available. It has been found of great advantage to continue such subjects as anatomy and pathology throughout the training period of the resident. It is too well known that cold anatomy, unaccompanied by clinical practice, is soon forgotten. On the contrary, the anatomy that must be learned preceding each operation and that must be reviewed following each problem is the anatomy that sticks in one's mind. It is my plea, therefore, that a concerted effort be made at the present time to afford each resident in otolaryngology an opportunity for the study of basic science throughout his entire course of training in the hospital. I believe the student is best prepared by constant and continuous application of the basic sciences to the clinical aspect of the specialty. Whatever method is pursued in training, the Board will always see that the student is properly qualified before certification. There is every reason to look forward to a great future in the prevention and treatment of disease in the field of otolaryngology.

1136 West Sixth Street.

---

## NEUROSURGERY (AND THE NEUROSURGEON) IN WORLD WAR II

R. GLEN SPURLING, M.D.
Louisville, Ky.

Most physicians who were actively engaged in the medicomilitary activities of World War II are one in their desire to dismiss the whole episode from their minds and fix their attention on new horizons. The physicians who were not active participants in those activities must be weary with hearing about them, for the progress of military medicine has been widely publicized. I therefore approach my subject, neurosurgery (and the neurosurgeon) in World War II, with some degree of trepidation. On the other hand, I think it will be profitable for all neurosurgeons, whether or not they participated actively in the medicomilitary phases of the war, to consider soberly and carefully the progress of this specialty during the four years of hostilities and in the period of so-called peace which came to pass when fighting ceased, as well as to reflect on the role of the civilian neurosurgeon in the Army in time of war.

Contrary to prewar predictions, injuries to the nervous system constituted nearly 10 per cent of all battle casualties. In numbers, in seriousness of the injuries and in the duration of treatment the neurosurgical load was second only to the orthopedic load. It is impossible now—and perhaps will never be possible—to determine accurately the number of major neurosurgical casualties which occurred in World War II. There were nearly 61,000 admissions to the neurosurgical centers in the Zone of the Interior, and it is likely that the over-all figure for these injuries was close to 100,000.

Read before the Section on Nervous and Mental Diseases at the Ninety-Sixth Annual Meeting of the American Medical Association, Atlantic City, N. J., June 12, 1947.

The management of a neurosurgical load of this size was a colossal task. It was difficult because of its magnitude and because competent neurosurgeons are not numerous. It was made more difficult—and unnecessarily difficult—by certain circumstances on which I shall comment later. But from every standpoint the task was well done.

The success of the neurosurgical therapeutic methods employed in World War II has already been recorded in the literature, and the details need no repetition. My purpose in this paper is twofold: (1) to summarize the procedures and policies in the major categories of neurosurgical endeavor, that is, head injuries, spinal cord injuries and peripheral nerve injuries, particularly as they differed from previous civilian procedures, and (2) to analyze briefly the role of the civilian neurosurgeon in the United States Army during World War II and in the future.

### THERAPEUTIC POLICIES AND PROCEDURES

*Head Injuries.*—The management of acute penetrating wounds of the brain in World War II followed, with no important modifications, the basic concepts formulated by the late Harvey Cushing for the management of those injuries during World War I. Unlike the neurosurgeons of that war, however, the neurosurgeons of World War II had almost perfect control of the infections which seemed inevitable in the earlier war. Thanks chiefly to chemotherapy, to liberal quantities of whole blood and blood plasma and to rapid evacuation by air, it was possible to make adaptations of those principles to military and tactical circumstances which even Cushing, with his imaginative outlook on neurosurgical problems, could not have dreamed possible in 1917 and 1918.

The neurosurgeon of World War II soon learned that unless the patient's condition was deteriorating it was not necessary to hurry him into an emergency operation for a penetrating wound of the brain. The front line surgeon, therefore, was able to concern himself with urgent cases, in which delay could not be tolerated, for he could with a clear conscience send the patients whose need was less urgent to hospitals in the rear for definitive surgical treatment. This policy reduced morbidity and saved lives. Moreover, it was of great usefulness from the tactical point of view, since it kept beds in the forward zone cleared for urgent casualties.

An important technical advance in the surgical treatment of penetrating wounds of the brain was the introduction of tantalum plate. Most casualties who survive this type of wound are left with unsightly scars and deformities from cranial defects, for which reconstructive surgical intervention is necessary. Cranioplasty with tantalum seems completely to have solved this problem. Preliminary work had been done with tantalum in civilian neurosurgery prior to the war, but Army neurosurgeons perfected the technic of the method and expanded its usefulness far beyond anything that had been achieved in civilian practice.

A second important development in respect to penetrating wounds of the brain is still in progress. Epilepsy is a not infrequent sequel of this type of wound, and there is much left to be learned about it. After the war had ended, the Surgeon General accepted the sug-

gestion of Army neurosurgeons that epileptic patients be concentrated in a specialized center, where they could be intensively studied. Under the direction of Dr. A. Earl Walker such a center was established at the Cushing General Hospital and was in operation until the fall of 1946, when it was taken over by the Veterans' Administration. During the period of its operation intensive studies were made on some 300 patients with post-traumatic epilepsy. At the present time, under the direction of Dr. Walker, four other post-traumatic epileptic centers are being established in general hospitals operated by the Veterans' Administration, and the work begun at the Cushing General Hospital Epileptic Center will be carried forward in them. The importance of this work, not only for military casualties but for further scientific observations under controlled conditions, needs no emphasis.

*Spinal Cord Injuries.*—One of the most important and certainly the most dramatic development in military neurosurgery in World War II was the program for the care and rehabilitation of patients with injuries of the spinal cord, though by no means all the credit for it belongs to the neurosurgeons. In the acute phases of their injuries these casualties were primarily neurosurgical problems, and neurosurgeons saw to it that every man with a penetrating wound of the spine associated with paralysis had the benefit of prompt surgical exploration by experienced personnel. Neurosurgeons, furthermore, worked unceasingly to expedite the transportation of these patients from forward hospitals to rear echelon installations properly equipped for their treatment. One can fairly say that the reason that so many of these tragically wounded men are alive and rehabilitated today is because of the unending efforts of all concerned in their care to supply prompt and expert treatment to them in the first phases of their injuries.

As soon as possible after operation paraplegic patients were evacuated to the Zone of the Interior, to specialized centers in general hospitals. Here a rehabilitation program was begun, based on well recognized policies effective in civilian clinics but applied with an efficiency and a zeal and a sympathetic understanding which surpassed any comparable previous effort. Much credit for its success belongs to the urologists, orthopedic surgeons, rehabilitation and dietary experts, physical therapeutists and other specialists who participated in it. The program was and is an example of medical and surgical cooperation and efficiency unique in both Army and civilian practice. The Veterans' Administration has taken it over, and some 1,200 paraplegic patients are now continuing their rehabilitation in five adequately equipped and staffed paraplegic centers.

The ultimate goal of the Army paraplegic program was that every patient should be able to resume his former place as an independent person in civilian life. Reach, quite naturally, exceeded grasp, but the rewards were nonetheless fruitful. Furthermore, the demonstration by the Army and the Veterans' Administration of what can be accomplished for paraplegic patients is gradually awakening the public to the civilian need for a similar program. In the United States today a thousand or more healthy young adults each year are suddenly rendered helpless by injuries to the spinal cord. At the present time it is next to impossible to find hospital space for them after the emergency phases of treatment have been completed. Modern rehabilitation facilities for civilians are practically nonexistent. The Army-Veterans' program is a challenge to civilian communities to provide adequate care for these unfortunate men and women, and to set as their goal the high standards established by the Army and Veterans' Administration in the paraplegic program.

*Peripheral Nerve Injuries.*—In one respect the most significant contribution made by Army neurosurgeons during World War II had to do with peripheral nerve injuries, for this is a problem which can be solved only in time of war. In peacetime the busiest civilian clinics do not see enough material of this sort to permit authoritative conclusions as to methods of management. In World War I the opportunity was there for the taking, but it was lost in spite of the numbers of peripheral nerve injuries which occurred, because no accurate and comprehensive follow-up studies were made.

One of the earliest efforts of neurosurgeons in World War II was to see to it that the opportunity was not lost a second time. It has not been. Early in 1944 a Peripheral Nerve Registry was established through the efforts of Dr. Barnes Woodhall, and by October 1945, when registrations were discontinued, some 8,000 peripheral nerve sutures had been registered. The registry has been taken over by the Veterans' Administration, and regular assessments of the progress of regeneration will be made by competent and impartial observers in five specially equipped centers. The follow-up study is planned to cover a five year period. When once these statistics are completed and have been analyzed and interpreted, the results of peripheral nerve surgery in World War II will be unequivocally clear, and the pattern will be established for the proper management of similar civilian injuries.

Certain conclusions are possible even at this time. It has been established beyond all reasonable doubt that the optimum time to suture a divided peripheral nerve is within three to six weeks after wounding. It has been clearly established that by careful coordination of personnel and facilities the majority of peripheral nerve injuries can be given definitive treatment within that optimum time, even in an active theater of operations, regardless of whether or not a bone injury is present also. It has been clearly established that the time-honored custom of splinting an extremity because of damage to a major nerve trunk is, in the absence of an associated fracture, not only useless but actually harmful. It has been clearly demonstrated that by early application of competent physical therapy the fixed, ankylosed joint which had previously been the surgeon's bugbear in the management of all paralyzed extremities will almost never develop.

In another field of peripheral nerve surgery it has been established beyond all reasonable doubt that grafting of large nerve defects in the human subjects by either autogenous or homogenous grafts was as unsuccessful in practice as it was fallacious in concept. All methods and technics were tested, and the results were uniformly bad. The question may be asked why a record of failures is emphasized. The reply is that had not the ineffectiveness of nerve grafting been settled conclusively and settled early in the war, many patients would have been treated by this inefficient method and would have lost the chance of nerve regeneration which is possible by better technical methods. As it

was, neurosurgeons learned, without delay, how to overcome large gaps in nerves by other means than grafting, including, as a last resort, shortening the bone of a paralyzed extremity.

### THE CIVILIAN NEUROSURGEON IN THE ARMY

Shortly after the United States entered World War II, it became my duty, as Consultant in Neurosurgery to the Surgeon General, to mobilize from civilian sources for military purposes all available neurosurgical talent. I knew then, though I did not comprehend the implications of the fact, that as of February 1942 there were in the United States only one hundred and fifty-four certified neurosurgeons. The significance of the number became apparent when I found that to meet the Tables of Organization of Army hospitals would have stripped every civilian clinic of its neurosurgical personnel and still would have left the Army short.

Army needs had to be met, and the most practical solution was to train young general surgeons in the principles of neurosurgery and to train them as quickly as possible. A program of instruction was at once set up consisting of two parts. The first part, didactic lectures and anatomic dissections, lasting a month, was originally at the Columbia University College of Physicians and Surgeons and was later transferred to the University of Pennsylvania School of Medicine. The second part consisted of clinical training in the neurosurgical centers in the United States. The students, at the conclusion of their didactic and laboratory work, were sent in small numbers to each of these centers and there, by lectures, instruction in the operating theater and ward work, they were taught the practical aspects of traumatic neurosurgery. When this training period, which lasted for three months, was completed, they were assigned to evacuation and general hospitals and to auxiliary surgical groups. Approximately two hundred young general surgeons were thus trained, and the exceptionally fine service which they rendered is the background of the unprecedentedly good care which neurosurgical casualties were given in World War II. Without them it could not possibly have been accomplished.

This demonstration of the possibilities of rapid training of specialists is, to my mind, one of the major medical accomplishments of World War II. If this method is applicable to the training of neurosurgeons in wartime, it should be equally applicable to the training of other surgical specialists in an emergency. The possibility is significant from the military point of view, and it has its lessons for civilian neurosurgery. In the prewar years there was a decided tendency in all surgical specialties, including neurosurgery, to underestimate and even belittle the value of a sound background in general surgery. As the result of the war experience it can be definitely said that a background of this sort is highly important in the training of civilian neurosurgeons and that in time of war it is essential.

In spite of the excellent neurosurgical results achieved in World War II, I should be less than honest if I permitted you to believe that I am fully satisfied with them. I am not. I doubt that any military neurosurgeon—certainly any neurosurgeon who was responsible for the development of clinical policies—is fully satisfied with them. It is a comfort to believe that we did as well as we could under the circumstances. But we should have done better. I base that statement on a number of considerations, about which I propose to speak frankly.

First of all, the question arises as to why approximately three hundred neurosurgeons were needed for 11,000,000 troops when several times as many civilians had been getting along very well with less than half as many. The obvious answer is that during wartime casualty rates far exceed the rates usual in peacetime. Analysis of the casualty figures confirms the observation but makes clear that it is not the whole answer. The most reasonable explanation is that under the Army system which existed in World War II efficient use was not made of neurosurgical personnel or, indeed, of the personnel in any other of the critical specialties. Such personnel was in short supply throughout the war. Yet it need not have been. Neurosurgical shortages developed because the Medical Department operated under the Army Service Forces, which is a service of supply, and because, as a result, medical personnel was handled, from an administrative point of view, exactly as rations, guns, clothing, food and other supplies were handled. Let me assure you that that is not the way to distribute medical personnel.

A second reason for shortages in neurosurgical personnel is that the channels of command were too complicated and too cumbersome to permit of efficient operation. I am fully aware that it is necessary in wartime to decentralize authority, especially in theaters of operations, but that awareness does not prevent me from also being aware that medical personnel in short supply cannot be efficiently utilized by nonmedical commands which, with all the will in the world, cannot comprehend or visualize medical needs and medical problems.

I had the responsibility, in the Zone of Interior and later in the European Theater of Operations, of seeing to it that neurosurgical casualties received competent neurosurgical care. The Army system made it an unnecessarily difficult task. My experience—and it was not unique—was to the effect that every time a new command was established, it became one more echelon of resistance to the proper allocation and distribution of medical talent. It was to the effect that every new commander who entered the picture, whether he was a base section surgeon or commanding officer of a hospital or of a hospital center, held on tightly to all the personnel in his command whether it was needed there or whether it was not. As a consequence, many critical specialists terribly needed elsewhere were frozen in commands and were unemployed for weeks or months at a time when they could have been doing vital work in the care of neurosurgical casualties.

To substitute constructive for apparently destructive comment, let me suggest a simple solution for this problem, based on recognition of the fact that critical specialists will always be in short supply and that their services must be utilized on that concept. I would not list a neurosurgeon, or any other critical specialist, on the Tables of Organization of any field, evacuation, general or station hospital, for two good reasons. The first is that all such units are necessarily deactivated, even when fighting is heavy, for longer or shorter periods, and that during these times specialists cannot function and are therefore lost to the Army. The second is that when once a medical officer appears on the Tables of Organization of a given unit it is a major operation to detach him from it.

My suggestion is to make neurosurgeons, and all other critical specialists, members of teams which are completely mobile and so entirely self contained that all of them can be moved at a few hours' notice from one location to another as the need for their services arises. They can be moved by small plane or by command car. Standard operating supplies are always available at all Army installations, and the only impedimenta which the team would need to carry with it would be its own specialized equipment.

It is true that neurosurgeons were attached to auxiliary surgical teams in World War II, but auxiliary teams were just that—auxiliary. By the plan which I propose these teams would cease to be supplemental. They would replace the specialized personnel hitherto attached to various types of installations and, if not entirely wasted in them, at least not used to the fullest possible advantage.

In the volumes on neurosurgery shortly to be published by the Surgeon General's Office as part of the medical history of World War II we have tried to present the operational and clinical material which I have discussed, and other matters of like importance to the meditomilitary future of the country, as fully and fairly as possible. We who provided the neurosurgical care for the casualties of that war owe it to those who will come after us to record, as faithfully and honestly as we can, our errors as well as our achievements, the difficulties under which we labored and whence they arose, the problems which we encountered and the solutions which we found for them during the war or which, in the light of experience and reflection, we would now suggest for them. If the neurosurgical history of World War II is written from this point of view, and if it is made compulsory reading for the neurosurgeons of any future war, then our successors will enter on their tasks equipped for them as we of World War II were not equipped for ours.

## ABSTRACT OF DISCUSSION

DR. BARNES WOODHALL, Durham, N. C.: I find it difficult to discuss Dr. Spurling's statement or to amplify it because of the fact that it lies outside of my own personal knowledge. However, on many occasions Dr. Spurling and I have discussed the possible place of neurosurgery and neurology in the event of another conflict. Although many answers cannot be given at this time, it seems to me that at least two things can be discussed, and perhaps some action taken. The first has to do with this annoying problem of specialized personnel, and I think the problem can best be illustrated by reference to the case of a colleague of mine. You will recall that many of the neurosurgeons left early in the university units, and Dr. Spurling had to get the remainder. This colleague was removed from the reserve corps because he was on the dean's essential list, and he was unfortunate enough to encounter Dr. Spurling at a hotel in Chicago. Some hours later, about 3 o'clock in the morning, after sufficient inducements, he found himself back in the Army. That is a hard way to secure neurosurgical personnel. I feel that one thing can be done, and that is that our boards can get in touch with the Pentagon, and perhaps maintain an up-to-date list of neurosurgeons who are available, because of their strong backs, for military duty, and others who might be available for total civilian care. The second point has to do with the relationship between neurosurgeons and neurologists in the military structure. As you know, there were no neurosurgeons when the war began; there were only septic surgeons in their place, and Dr. Spurling traded the classification in the Army organization table, and furthermore the neurologist was on the medical side and the neurosurgeon was on the surgical side. There was only one hospital in this country in which neurologists and neurosurgeons worked together, both being specialists interested in organic diseases of the brain. This coordination was achieved only at the expense of a considerable "rumpus," involving even the Surgeon General. This is the one hospital that achieved great things in the efficient care of patients and in promoting clinical investigation. As many of you know, I am referring to the Cushing Hospital. Certainly the tables of organization should be changed so that the neurosurgeon and the neurologist may work together and may be free of this baneful influence of the general surgeon and the general internist. Dr. Spurling did not mention the driving force behind these accomplishments, but I am happy to name the driving force and to add that Dr. Spurling achieved a place in military neurosurgery in World War II that can only be compared with the place that was achieved by his chief, Dr. Cushing, in World War I.

# ULTRAVIOLET IRRADIATION OF HUMAN PLASMA TO CONTROL HOMOLOGOUS SERUM JAUNDICE

ALBERT M. WOLF, M.D.
JACK MASON, M.D.
WILLIAM J. FITZPATRICK, M.D.
STEVEN O. SCHWARTZ, M.D.
and
SIDNEY O. LEVINSON, M.D.
Chicago

Numerous publications [1] have established that human blood, plasma or serum may harbor the agent of infectious hepatitis. This agent, believed to be a virus, has been the cause of hepatitis in recipients of human blood and plasma.[2] Because of the prolonged incubation period—two to six months—the relationship between administration of blood or plasma and the subsequent development of hepatitis is frequently overlooked.

It is easy to exclude blood donors with a history of jaundice or hepatitis and to discard blood specimens showing hyperbilirubinemia. Unfortunately, however, many persons may be unknowingly infected, for many cases of hepatitis occur without the development of typical symptoms and signs and thus pass undiagnosed. Furthermore, the virus may be present in the blood stream of the infected person for weeks before and after the acute episode of hepatitis. It is clear that administration of human blood or plasma carries with it a potential hazard of hepatitis, despite careful selection of donors.

In the absence of a satisfactory method or test for recognizing and excluding such infected blood, it is obviously desirable that all human blood plasma and serum be treated to destroy the virus of infectious hepatitis and protect the recipient of these materials from the hazard of hepatitis. Any proposed method must meet at least three criteria: 1. It must destroy the virus. 2. It must be free of harmful side effects. 3. It must be practical.

A new method of rapidly sterilizing suspensions of bacteria and viruses has been developed by Oppen-

From the Samuel Deutsch Serum Center of the Michael Reese Research Foundation, and the Hektoen Institute for Medical Research of the Cook County Hospital.

Dr. Milton V. Veldee, Chief of the Biologics Control Laboratory of the National Institute of Health, Bethesda, Md., contributed valuable suggestions on carrying out this study.

1. Neefe, J. R.; Gellis, S. S., and Stokes, J., Jr.: Homologous Serum Hepatitis and Infectious (Epidemic) Hepatitis, Am. J. Med. **1**: 3 (July) 1946.

2. Paul, J. R.; Havens, W. P., Jr.; Sabin, A. B., and Philip, C. B.: Transmission Experiments in Serum Jaundice and Infectious Hepatitis, J. A. M. A. **128**: 911 (July 28) 1945.

heimer and Levinson.[3] This new method consists essentially of exposing rapidly flowing thin films of liquid for fractions of a second to a new and powerful source of ultraviolet emitting intense radiation of 2,537 angstrom and 1,849 angstrom wavelengths.

Oliphant [4] reported that serum infected with hepatitis virus and treated by this method was rendered free of the agent. Since the Oppenheimer-Levinson equipment is effective in destroying virus and since it is capable of irradiating large quantities of serum and plasma, it appeared that irradiation could be applied to plasma and serum if it had no deleterious effects on the plasma itself. The data herein presented represent a preliminary report of our studies to determine whether irradiated plasma is free of side effects from irradiation and whether it is satisfactory for human use.

The effects of irradiation of rabbit plasma were first tested. Rabbit plasma was pooled and divided into three portions, one of which served as nonirradiated control, one was irradiated for one second, and another for two and one-half seconds. Rabbits were given injections of 10 cc. per kilogram of body weight intravenously, as indicated in table 1. All of the rabbits tolerated the injection well. These results showed no evidence of toxicity from irradiation and seemed to justify experimental work with human plasma.

TABLE 1.—*Effects of Irradiation on Rabbit Plasma*

| | Ultraviolet Exposure | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | None | | | | 1 Second | | | | 2.5 Seconds | |
| | Rabbit 1 | Rabbit 2 | Rabbit 3 | Rabbit 4 | Rabbit 7 | Rabbit 8 | Rabbit 9 | Rabbit 10 | Rabbit 5 | Rabbit 6 |
| Temperature before injection | 102.0 | 101.5 | 102.2 | 101.5 | 102.1 | 102.1 | 102.3 | 102.1 | 101.6 | 102.6 |
| Temperature 1 hour after injection | 102.8 | 102.8 | 102.4 | 102.5 | 103.2 | 103.0 | 103.1 | 103.0 | 101.7 | 103.0 |
| Temperature 2 hours after injection | 102.6 | 102.6 | 102.4 | 102.6 | 103.0 | 103.0 | 102.9 | 103.0 | 101.9 | 103.2 |
| Temperature 3 hours after injection | 102.1 | 102.8 | 102.9 | 102.4 | 102.6 | 102.9 | 102.6 | 102.8 | 102.2 | 102.8 |
| Temperature rise | 0.8 | 1.3 | 0.7 | 1.1 | 1.1 | 0.9 | 0.8 | 0.9 | 0.6 | 0.6 |
| Average rise for group | 1.0 | | | | 0.9 | | | | 0.6 | |

A small pool consisting of 2 liters of human plasma prepared from the blood of normal, healthy adults was irradiated, an exposure of one second being used. This exposure time was much longer than necessary to inactivate other viruses in past experiments. Three patients received 250 cc. each and a fourth received 500 cc. After administration, none of the 4 patients showed any reaction which would not fall well within the normal range.[5] These favorable results called for more extensive testing of irradiated plasma.

Plasma lot PT-4652, consisting of approximately 9 liters of human plasma prepared from the blood of normal, healthy adults, was processed in strict accordance with the requirements of the National Institute of Health, except for the additional step of irradiation, introduced just before bottling in final containers. The plasma was irradiated for approximately one-third second (an exposure time adequate to inactivate other virulent virus suspensions). A specimen was saved from this pool to serve as a nonirradiated control. The irradiated plasma on inspection showed no change in color and no change in general appearance. Specimens of the irradiated plasma were inoculated into mice and guinea pigs, which tolerated the injections well. Each of 3 rabbits was given an intravenous injection of 5 cc. of the irradiated plasma, and none showed any reaction or significant rise in temperature in the succeeding three hours. Electrophoretic studies of the irradiated human plasma and the nonirradiated control material were made.[6] The results showed "no consistent variation between irradiated and nonirradiated samples."

TABLE 2.—*Clinical Results with Irradiated Human Plasma (PT-4652)*

| No. of Cases | Intravenous Injections, Cc. | Rate of Injection, Cc./Min. | Rise in Temperature | Comment |
|---|---|---|---|---|
| 9 | 300 | 5 to 10 | None | No evidence of reaction |
| 1 | 350 | 6 | None | This patient, asthmatic with osteomyelitis of the hip, experienced urticaria of face and chest |
| 6 | 600 | 7½ to 10 | None | No evidence of reaction |
| 1 | 900 | 12 | None | No evidence of reaction |

Human beings have received injections from this lot of irradiated human plasma, with the results shown in table 2. Twenty-one patients received irradiated plasma in dosage from 250 to 900 cc. One patient experienced urticaria, a reaction encountered when untreated blood or plasma is used. No other reaction was observed.

It may, therefore, be tentatively concluded that controlled ultraviolet irradiation would appear to be a practical, yet harmless and safe, procedure which will free plasma (or serum) from the hazard of transmitting infectious hepatitis.

3. Oppenheimer, F., and Levinson, S. O.: A New Method for the Production of Potent Inactivated Vaccines with Ultraviolet Irradiation: I. Principles, Technique and Apparatus. (Publication withheld by the Committee on Medical Research of the Office of Scientific Research and Development, Washington, D. C.). Levinson, S. O.; Milzer, A.; Shaughnessy, H. J., and Neal, J. L.: A New Method for the Production of Potent Inactivated Vaccines with Ultraviolet Irradiation: II. Sterilization of Bacteria and Immunization with Rabies and St. Louis Encephalitis Vaccines, J. Immunol. **50**: 317 (June) 1945. Milzer, A.; Oppenheimer, F., and Levinson, S. O.: A New Method for the Production of Potent Inactivated Vaccines with Ultraviolet Irradiation: III. A Completely Inactivated Poliomyelitis Vaccine with the Lansing Strain in Mice, ibid. **50**: 331 (June) 1945.

4. Oliphant, J. W.: Jaundice Following Administration of Human Serum, in Harvey Lectures, 1943-1944, Lancaster, Pa., Science Press, 1944, vol. 39, p. 254.

5. These tests were done at the Gallinger Hospital at the request of Dr. Milton V. Veldee of the National Institute of Health, who reported the results to us in a personal communication.

6. The Research Department of the Armour Laboratories performed these studies.

**Aniseikonia.**—There are twenty-one aniseikonia clinics in the United States. In our general population as many as two million persons may have complaints correctable by aniseikonic glasses which would otherwise remain unrelieved. This means that about 5 per cent of those wearing glasses would be benefited by aniseikonic correction. It may be years before enough refractionists obtain the instruments and acquire the experience necessary to prescribe successfully for this condition. In the meantime it is important for the refractionist to recognize which of his patients he should refer for aniseikonic study.—Miles, Paul W.: Factors in the Diagnosis of Aniseikonia and Paired Maddox Rod Tests, *Am. J. Ophth.* **30**:885 [July] 1947.

# ANTIBIOTICS AND TUBERCULOSIS

## A Microbiologic Approach

SELMAN A. WAKSMAN, D.Sc., Ph.D.
New Brunswick, N. J.

The recent interest in the production, isolation and utilization of antibiotic substances for the treatment of infectious diseases, especially the recognition of the fact that certain antibiotics, notably streptomycin, may find an important place in the treatment of tuberculosis, has suggested the advisability of reviewing the accumulated information on the effect of antagonistic micro-organisms and their metabolic products on Mycobacterium tuberculosis, the causative agent of human and animal tuberculosis.

Surprisingly enough, the interest in the possibility of suppressing the growth of the tubercle bacillus and of alleviating the disease caused by it date back to the early days of bacteriology. Numerous reports have been published which tended to emphasize the fact that a large number of micro-organisms, both saprophytic and pathogenic in nature, exert a pronounced effect on this bacillus.

The first attempt to treat clinical tuberculosis by means of nonpathogenic bacteria was made within three years after Robert Koch first isolated the organism responsible for this disease and within one year after this organism, which came to be generally known as Koch's bacillus, was described. The credit for the first application of bacteriotherapy to tuberculosis must go to Cantani.[1] On the basis of previous observations that the virulence of tuberculosis in corpses disappeared under the influence of putrefactive processes, Cantani in 1885 conceived the idea of treating pulmonary tuberculosis by having the patient inhale cultures of nonpathogenic bacteria. A common saprophytic organism known as Bacterium termo was used for this purpose. A woman aged 42, who had a large cavity in the superior lobe of the left lung, who suffered from fever and coughing and whose sputum test was positive, was treated by inhalation of a liquefied gelatin culture of the saprophyte, diluted with meat broth. The pathogenic organisms in the sputum were rapidly reduced in numbers and eventually disappeared completely; the fever diminished, and the patient's condition improved.

It may be of interest to quote from the original paper by Cantani, in which he expressed his ideas on the subject of bacteriotherapy and reported the results obtained in the treatment of this particular patient:

> The well known fact that certain bacteria may destroy the culture of others and also particularly of pathogenic schizomycetes, provided that they may get inside of them, suggested to me the idea of using this experience for therapeutic experiments in various infectious diseases. The first experiment was aimed at tuberculosis. I first selected Bacterium termo to combat the tuberculosis bacillus of Koch. . . . Herewith I made my first experiments on human tuberculosis. On May 4 inhalations of a pure culture of B. termo in liquefied nutrient gelatin which had been diluted with meat broth were started by means of a spray apparatus with a double rubber balloon. The expectoration decreased rapidly, and finally it ceased completely during the last days of the experiment. The number of tubercle bacilli decreased likewise, while B. termo could be demonstrated in the sputum; on June 1 the tubercle bacilli had disappeared completely from the sputum and could no longer be demonstrated while B. termo were observed in increasing numbers. There was a drop in temperature so that during the last days (of the experiment) the evening temperature no longer reached 100.4 F. (38 C.); the body weight was increased again to 39.6 Kg. The patient looked considerably better, the general condition was satisfactory; the subjective feeling of strength was improved considerably. Animals which were inoculated with the sputum (which was free of tubercle bacilli on microscopic examination) did not manifest any symptoms of tuberculous disease.
>
> (Die bekannte Tatsache, dass gewisse Bakterien die Culturen anderer und namentlich auch pathogener Schizomyceten zerstören, wenn sie auf irgend eine Art in dieselben gelangen, brachte mich auf die Idee, diese Erfahrung für die Therapie verschiedener Infectionskrankheiten experimentell zu verwerten. Mein erster diesbezüglicher Versuch war auf die Tuberculose gerichtet, und wählte ich zunächst Bacterium termo, um damit den Bacillus tuberculosis Koch zu bakämpfen. . . . Hiermit führte ich meinen ersten Versuch am kranken Menschen aus. Am 4. Mai begannen die Inhalationen einer Reinkultur von Bacterium termo in verflüssigter mit Fleischbrühe verdünnter Nährgelatine mittels eines Zerstäubungsapparats mit doppelter Kautschukblase. Die Expectoration nahm rasch ab, bis zum gänzlichen Aufhören in den letzten Tagen des Experiments; die Tuberkelbacillen nahmen gleichfalls baldigst ab, während B. termo darin nachweisbar wurde; am 1. Juni fehlten die Tuberkelbacillen vollständig im Auswurf, und kamen nicht mehr darin vor, während B. termo in immer grösserer Quantität darin vorhanden war. Das Fieber nahm ab, so dass in den letzten Tagen der Beobachtung die Abendtemperatur nicht mehr 38 C. erreichte, und das Körpergewicht nahm wieder bis auf 39.6 Kg. zu; das Aussehen der Kranken war sehr gebessert, der Allgemeinzustand lobenswert, das subjective Kraftgefühl bedeutend gehoben. Tiere, denen die nun mikroskopisch an Tuberkelbacillen freien Sputa inoculirt wurden gaben kein Zeichen tuberculoser Erkrankung.)

Cantani did not claim that the saprophytic B. termo would destroy the deeply infiltrated tubercle bacilli. He merely extended hope that this first experiment might lead to the isolation of other bacteria which would be used in combating various pathogenic organisms. In commenting on Cantani's experiments Babes[2] suggested in the same year that it would have been advisable before determining the therapeutic effect of one microbe on another in vivo to test such effects by pure plate cultures on gelatinized mediums.

Soon afterward, in 1888, Babes[3] demonstrated that products of various saprophytic organisms, such as the pyocyaneus, tetragenus, staphylococcus and diplobacillus, have the capacity of inhibiting the growth of tubercle bacilli; streptococci, however, appeared to be favorable to the development of the tuberculosis organism. The importance of associative organisms in influencing the course of tuberculosis was thus emphasized.

Somewhat later, in 1893, Nannotti[4] observed that tubercular inflammation of the knee joint tended to subside as a result of the spontaneous occurrence of erysipelas. The use of streptococci or their metabolic products, filtered and sterilized, resulted in a modification of the tuberculous process; abscesses grew smaller and fistulas tended to heal. These studies led Prudden[5] soon afterward to the conclusion that there

Read at the presentation of the Passano Award in Atlantic City, N. J., on June 11, 1947.

From the Department of Microbiology, New Jersey Agricultural Experiment Station, Rutgers University.

Journal Series Paper, New Jersey Agricultural Experiment Station, Rutgers University, Department of Microbiology.

1. Cantani, A.: Versuch über Bacteriotherapie, Centralbl. f. d. med. Wissensch. **23**: 513-515, 1885.

2. Babes, V.: Concurrence vitale des bactéries: Atténuation de leur propriétés dans des milieux nutritifs modifiés par d'autres bactéries; tentatives de thérapeutique bactériologique, J. d. conn. méd. prat. **7**: 321-323, 1885.

3. Babes, V.: Sur les associations bactériennes de la tuberculose. Congr. p. l'étude de la tuberc., 1888, pp. 542-560.

4. Nannotti, A.: Osservazione clinica e ricerche sperimentali intorna alla influenza delle infiammazioni da streptococco nelle affecioni tubercolari, abstracted, (Centralbl. f. Bakt. **14**: 601-602, 1893).

5. Prudden, M.: Concurrent Infection and Formation of Cavities in the Acute Pulmonary Tuberculosis, New York M. J. **40**: 1-11, 1894.

was no evidence of a specific antagonism of a certain organism toward the tubercle bacillus; the results obtained by Nannotti may have been due to simple inflammation caused by the accompanying organisms.

Prudden also observed that the presence of streptococci in pulmonary tuberculous infections modified considerably the course of the disease. Highly suggestive results were obtained in culture; namely, the growth of the streptococci prevented the subsequent development of the tubercle organism. Prudden elucidated these results succinctly as follows:

> When the tubercle bacillus and the Streptococcus pyogenes are planted together on glycerinated (5 per cent) beef broth, the streptococcus grows as abundantly as in separate control cultures, while the tubercle bacillus does not grow at all. On the glycerinated broth, in which the streptococci had grown for five days, and which was rendered sterile by filtration through porcelain, the tubercle bacillus failed altogether to grow, either when the sterilized broth was used in its full strength, or when diluted in various degrees down to four times its volume with fresh glycerinated broth.

Although the culture filtrate of the tubercle organism also had an inhibiting effect on the growth of the streptococcus, this effect was of much lesser magnitude.

These early clinical and laboratory studies on the antagonistic effects of various micro-organisms and their metabolic products on the growth of Myco. tuberculosis in culture and on the course of the disease produced by this organism were later followed by more exact studies, both in vitro and in vivo. They finally culminated in the work of Rappin [6] on spore-forming bacteria and of Vaudremer [7] on fungi which tended to establish the sensitiveness of the tubercle bacillus to the products of various organisms. This work done between 1910 and 1913 ended the first period of study of the antagonistic effects of various micro-organisms on tubercle bacilli; it also established definitely that not only living microbes but their products, now known as antibiotics, have the capacity of inhibiting and even destroying the tubercle organism both in the test tube and in the living body. Hope was thus aroused that in time a practical agent would be found for the treatment of this important and widespread disease, which has long been known as the white plague of mankind.

Before proceeding to analyze the results of the more recent investigations, especially the effects of antibiotics on tuberculosis, it may be of interest to examine certain pertinent information concerning the survival of Myco. tuberculosis in the soil and in other substrates and the production of antituberculosis agents or tuberculostatic and tuberculocidal substances by micro-organisms.

## SURVIVAL OF MYCOBACTERIUM TUBERCULOSIS OUTSIDE THE HOST

The fate of the organism causing tuberculosis outside the human or animal host has received much consideration. Difficulty has frequently been encountered in demonstrating the presence of the tubercle bacillus in a given natural substrate, such as soil and water, because of lack of suitable methods and the need for animal inoculation in order to establish the true pathogenic nature of the organism. The survival of Myco. tuberculosis outside the host was found to be affected by light and by increased temperature; it was greater in the dark than in diffused light and greater at a lower than at a higher temperature.

When a culture of the bovine strain of Myco. tuberculosis was mixed with cow manure and exposed in a 2 inch (5 cm.) layer in a pasture, it remained virulent for two months in sunlight and longer in the shade. The organism was still alive on the two hundred and thirteenth day and was dead on the two hundred and thirtieth day. In running water the cells survived for more than a year.[8] It was gradually recognized that the presence and activity of nonpathogenic micro-organisms greatly affect the life of the tubercle bacillus outside the host. The pathogen survived, for example, for three hundred and nine days in sputum kept in darkness even when completely desiccated. In decomposing sputum, however, it could be isolated after twenty days but not after twenty-five days. It remained alive and virulent in cow's feces exposed on pasture land for at least five months during the winter, two months during the spring and four months during the autumn; in the summer, however, no living tubercle bacilli could be demonstrated even after two months. Feces protected from earthworms yielded viable cells even after five months.

The addition of manure to soil was believed to favor the survival of the tubercle bacillus, as indicated by the fact that a higher proportion of test animals became tuberculous when the amount of manure added to the soil was increased.[9] The presence of the organism in soil and in manure was established even after one hundred and seventy-eight days but not later. On grass the organism survived for at least forty-nine days. Rhines [10] found that Myco. tuberculosis multiplied in sterile soil as well as in the presence of certain pure cultures of bacteria; however, a certain unidentified fungus was able to check the development of the pathogen, especially in manured soil. In nonsterile soil the pathogen was slowly destroyed, the plate count being reduced in one month to about one sixth of the original. Numbers of an avian strain of the tubercle bacillus were reduced in seventy-three days from 48,000 to 1,400 cells per cubic centimeter in sewage and to 4,200 in stream water.[11]

## PRODUCTION OF ANTIBIOTIC SUBSTANCES BY MICRO-ORGANISMS

Every investigator of the organism causing tuberculosis observed at one time or another that when his cultures became contaminated with molds or with bacteria the culture of the pathogen no longer grew. This inhibiting effect was believed to be due to competition for nutrients or for oxygen, or to the formation by the invading saprophyte of growth-inhibiting substances which affected the pathogen.

It was gradually established that the production of antituberculosis or tuberculostatic and tuberculocidal agents is widespread among micro-organisms; that these agents, or antibiotics, are active against various acid-fast bacteria, and that they are produced abundantly by various members of all major groups of micro-organisms, namely, fungi, bacteria and actinomycetes.

6. Rappin, M.: Action exercée par les diastases de quelques espèces saprophytes sur la tuberculose expérimentale du cobaye, Gaz. méd. de Nantes 1912, pp. 958-960.

7. Vaudremer, A.: Action de l'extrait filtre d'Aspergillus Fumigatus sur les Bacilles Tuberculeux, Compt. rend. Soc. Biol. **74**: 278-280 and 752-754, 1913.

8. Briscoe, C. F.: Fate of Tubercle Bacilli Outside the Animal Body, Bulletin 161, Illinois Agricultural Experiment Station, 1912, pp. 279-375.

9. Maddock, E. C. G.: Studies on the Survival Time of the Bovine Tubercle Bacillus in Soil, Soil and Dung, in Dung and on Grass, with Experiments on the Preliminary Treatment of Infected Organic Matter and the Cultivation of the Organism, J. Hyg. **33**: 103-117, 1933.

10. Rhines, C.: The Persistence of Avian Tubercle Bacilli in Soil and in Association with Soil Microorganisms, J. Bact. **29**: 299-311, 1935.

11. Rhines, C.: The Longevity of Tubercle Bacilli in Sewage and Stream Water, Am. Rev. Tuberc. **31**: 493-497, 1935.

Among the fungi, the Aspergillus fumigatus group received particular attention.[12] Although this organism produces four antibiotics, the active substance responsible for the antituberculosis effect appears to be fumigacin. Among the bacteria the Bacillus subtilis group was given special consideration, especially in recent years, with subtilin coming lately to the fore as a possible tuberculostatic agent. The actinomycetes have contributed several antibiotics active against tuberculosis, namely, actinomycin, streptothricin, streptomycin and nocardin. Among these, streptomycin is recognized to be the most promising therapeutic agent for the treatment of tuberculosis, because of its desirable physical and chemical properties, its low toxicity to animals and its pronounced effect on the tuberculosis organism both in vitro and in vivo.

## PRODUCTION OF ANTITUBERCULOSIS AGENTS BY FUNGI

Although it was known before the end of the last century that various fungi have the capacity of inhibiting the growth of and even of destroying various bacteria, it was not until 1913 that Vaudremer [13] first reported that certain fungi, comprising members of the Aspergillus (A. niger, A. fumigatus) and Penicillium groups, have a destructive effect on Myco. tuberculosis and that these fungi produce tuberculostatic and tuberculocidal substances. He was led to these studies by the observation that the fungi destroyed tuberculin, a phenomenon which he ascribed to the proteolytic activities of the organisms. Since tuberculin was considered as a toxalbumin, one of the constituents of the protoplasm of Myco. tuberculosis, a study was made of the effect of one of these fungi, A. fumigatus, on the tubercle bacillus. When virulent cells of this organism were suspended for twenty-four days at 39 C. in a filtered extract of A. fumigatus and the culture thus treated was inoculated into experimental animals, infection did not occur. The conclusion was reached that the fungus produced a thermostable substance, which was responsible for the antituberculous effects; this substance caused the lysis or digestion of the tubercle bacilli and rendered them nonpathogenic.

Vaudremer utilized the extracts of the fungus for the treatment of some 200 patients with tuberculosis. Although certain quite unexpected results were obtained, any conclusions based on them were considered as premature; however, the preparations appeared to be nontoxic. These results hardly justified any recommendation at that time that this method of treatment of tuberculosis be further extended. This is expressed emphatically in Vaudremer's paper:

> It is still too early to draw any conclusions with regard to the treatment of tuberculosis in man. Since 1910 we have treated more than 200 patients with extracts of A. fumigatus; the treatment was practiced in several hospitals and sanatoriums in Paris. From the facts observed one may conclude that these injections are innocuous, since they never caused a febrile reaction. Occasionally one even observes an unexpected recovery. In other cases one may observe a temporary improvement; but unfortunately the instances are still numerous in which tuberculosis takes its course.
>
> (Toute conclusion est également prématurée si on envisage le traitement de la tuberculose humaine. Depuis 1910, nous avons traité plus de deux cents malades avec les extraits d' *A. fumigatus*; le traitement a été appliqué dans plusieurs hôpitaux et sanatoriums parisiens. Des faits que nous avons observés, on peut conclure à l'innocuité de ces injections qui ne provoquent jamais de réaction fébrile. Parfois même on voit survenir des guerisons inespérées. Dans d'autres cas, on observe une amélioration passagère; mais malheureusement les faits sont encore nombreux où la tuberculose poursuit son évolution.)

Nearly a quarter of a century elapsed before fungi were again considered as organisms capable of producing substances that possessed antituberculosis properties. A real flow of contributions was started in 1940; Zorzoli [14] observed that various fungi including certain aspergilli and mycotorulae produced a thermostable substance which had a pronounced antibacterial effect on the human and bovine strains of Myco. tuberculosis. These results were confirmed by experiments in guinea pigs: when the tubercle organism was exposed for varying periods of time to the culture filtrates of the aforementioned fungi it lost much of its virulence to animals. The Oxford group [15] which investigated the potentialities of penicillin could not detect any inhibitory action of this antibiotic on the growth of the tubercle organism even in a dilution of 1:1,000.[15]

Soltys [12c] tested various fungi for their action against acid-fast bacteria; here again, A. fumigatus proved to be the most active organism. Unfortunately, he labeled the active filtrate aspergillin, a term previously used to designate the black pigment of A. niger. The antibiotic substance was thermostable, bacteriostatic rather than bactericidal, and active in a dilution of 1:10 to 1:20 against the human, bovine and avian strains of Myco. tuberculosis and in 1:50 to 1:100 dilution against Mycobacterium phlei.

Asheshov and Strelitz [12a] also observed a definite effect of A. fumigatus preparations on the Bacille Calmette Guérin strain but not on the avian strain of Myco. tuberculosis. The bacteriostatic action was greater against the former than against staphylococci, although the bactericidal capacity was lower. According to Jennings,[16] helvolic acid, or fumigacin, one of the antibiotics produced by A. fumigatus, completely inhibited the growth of the tuberculosis organism isolated from sputum in concentrations of 1:10,000. In 1:100,000 dilution the inhibition was only partial.

These results seem to point definitely to the fact that A. fumigatus is the organism of choice for the production of antituberculosis agents but other fungi also have tuberculostatic and tuberculocidal properties.

Aspergillus ustus produces an antibiotic that has the capacity of inhibiting the growth of Myco. tuberculosis and Mycobacterium ranae.[17] The active substance was extracted from the medium with ether as well as with other organic solvents. On evaporation of the solvent, the residue was dissolved in phosphate buffer of $p_H$ 11.0; on acidification, a yellow flocculent precipitate was obtained. The preparation was effective against Myco. ranae in a dilution of 1:150,000 to 1:300,000.

Aspergillic acid, a metabolic product of Aspergillus flavus, gave complete growth inhibition of a fast-growing strain of Myco. tuberculosis in a dilution of

12. (*a*) Asheshov, I. N., and Strelitz, F.: An Antibiotic Substance Active Against Mycobacterium Tuberculosis, Science **101**: 119-120, 1945. (*b*) Goth, A.: The Effect of Cobalt on the Antituberculosis Activity of Aspergillic Acid, Fed. Proc. **5**: 180, 1946. (*c*) Soltys, M. A.: Antibiotic Action of Aspergillus Fumigatus Against Mycobacterium Tuberculosis, Nature, London **154**: 550-551, 1944.

13. (*a*) Vaudremer, A.: Action de quelques microbes sur la tuberculine: Contribution a l'étude de la nature de la tuberculine, Ann. Int. Pasteur **24**: 189-195, 1910; (*b*) footnote 7.

14. Zorzoli, G.: Influenza dei filtrati di alcuni miceti sul Bacillo tubercolare umano e bovino. Ann. Inst. "Carlo Forlanini," **4**: 208-220 and 221-237, 1940.

15. Abraham, E. P.; Chain, E.; Fletcher, C. M.; Gardner, A. D.; Heatley, N. G.; Jennings, M. A., and Florey, H. W.: Further Observations on Penicillin, Lancet **2**: 177-189, 1941.

16. Jennings, M. A.: Activity of Helvolic Acid Against Mycobacterium Tuberculosis, Nature, London **156**: 633, 1945.

17. (*a*) Hogeboom, G. H., and Craig, L. C.: Identification by Distribution Studies: VI. Isolation of Antibiotic Principles from Aspergillus Ustus, J. Biol. Chem. **162**: 363-368, 1946. (*b*) Kurung, J. M.: Aspergillus Ustus, Science **102**: 11-12, 1945.

1:80,000 in broth, but it was not active in Long's synthetic medium.[18] The lack of activity in this medium was due to the presence of the ferric ion, which inactivated the antibiotic. It was suggested that iron is essential for the growth of Myco. tuberculosis and that aspergillic acid exerts an inhibiting effect on this organism by interfering either with the utilization of iron or with the functioning of an iron-containing enzyme system.[12b] Other strains of aspergilli were also found [19] capable of forming in synthetic mediums antibiotics active against the tuberculosis organism.

Although, as has been pointed out, penicillin has no tuberculostatic activity, ether extracts of the crude culture medium of Penicillium notatum were reported by Smith and Emmart [20] to exert a pronounced in vitro effect on the tubercle organism. A slightly favorable effect was obtained in the chorioallantoic membrane of the chick embryo and on guinea pigs. The extracts of another fungus, Penicillium cyclopium, were without effect, however, thus indicating that the production of the antituberculosis factor is characteristic of P. notatum.

More recently, however, penicillin itself, when used in concentrations of 20 to 80 Oxford units per cubic centimeter, was observed [21] to exert a bacteriostatic effect on freshly isolated strains of Myco. tuberculosis, but it was without effect on an avirulent laboratory strain; the latter actually had the capacity of destroying penicillin. When used in small amounts, penicillin may actually produce a favorable effect on the growth of the tubercle organism.

The Fusarium group of fungi also contains organisms that possess tuberculostatic properties. Carr [22] observed that a culture filtrate of Fusarium solani tested in vitro against the H 37 strain of human tuberculosis was found to decrease its vitality. An alundum capsule containing 5 cc. of medium was inoculated [23] with a culture of Fusarium and introduced into a 250 cc. Erlenmeyer flask containing 100 cc. of Long's medium, the latter being inoculated with a fresh virulent strain of the tubercle organism. The culture filtrate of the Fusarium was active in a dilution of 1:20, the substance being thermostable. A pigment, designated as javanicin, was isolated [24] from Fusarium javanicum; it was active in vitro against the human strain of Myco. tuberculosis in concentrations of 1:50,000 to 1:100,000; this pigment was relatively nontoxic.

Miller and Rekate [25] reported that culture filtrates and extracts of certain fungi were inhibitive to the tuberculosis organism. Gerber and Gross [26] designated one such extract mycocidin; its effect on the human strain of tuberculosis was both bacteriostatic and bactericidal.

Certain higher, or mushroom, fungi also produced antibiotics which possess antituberculosis properties. It is sufficient to mention clitocybin and nebularine. The first is a product of Clitocybe candida and Clitocybe gigantea; [27] it is soluble in water and in various organic solvents, such as ether, alcohol, acetone and chloroform; it is not particularly toxic, and it exerts both a static and a lytic action on the tubercle organism not only in vitro but also in vivo, in guinea pigs. The second antibiotic is found in the press juice of Clitocybe nebularis; it is a thermostable substance and is active on mycobacteria and Brucella abortus.[28] A pigment designated as lactaroviolin was recently [29] isolated from Lactarius deliciosus; the chemical composition of the substance was given as $C_{15}H_{14}O$; it inhibited the growth of Myco. tuberculosis in a concentration of 0.31 millimol per liter of medium.

Attention may be also called here to a phenomenon described as forced antagonism. By the use of a synthetic medium, with living tubercle bacilli as the only source of nitrogen (2 per cent sucrose and 0.1 mg. of living bacteria in 2 cc. of medium), Schiller [30] trained or forced beer yeasts to develop mechanisms which enabled them to digest the cells of the pathogen. In two days the yeasts developed and the tubercle organisms disappeared. The centrifuged medium contained an antituberculosis factor, since it had the capacity of rapidly digesting living tubercle bacilli, preceded by their agglutination. The tuberculolytic substance was thermolabile; its action was believed to consist in dissolving the wax of the bacterial cells. These results have never been confirmed; in one experiment the yeasts and fungi were actually superseded by the tubercle organism.[31]

This brief survey of the production by fungi of antibiotics active against tuberculosis justifies the conclusion that many are potentially active agents which vary greatly in their origin, chemical nature and activity in the animal body. Although none of these substances has so far achieved practical application for therapeutic purposes, there is hope that, in view of the relatively limited search which has been made to date, some compounds may still be found which can be utilized in one way or another—alone, as a supplement or in a modified chemical state—in the control of this disease.

## PRODUCTION OF ANTITUBERCULOSIS AGENTS BY BACTERIA

A brief survey of the production of antituberculosis substances by bacteria will also reveal many highly promising observations, although at some periods this subject seemed to have been completely neglected.

Since Babes first demonstrated experimentally in 1888 that certain bacteria have the capacity of influencing the growth of the tubercle bacillus, considerable evidence has accumulated. This was followed by various observations made by different investigators that the property exerted by saprophytic and pathogenic organisms on Myco. tuberculosis is not limited to cer-

18. Goth, A.: The Antitubercular Activity of Aspergillic Acid and Its Probable Mode of Action, J. Lab. & Clin. Med. **30**: 899-902, 1945.
19. Kallós, P.: Antibiotic Action of an Aspergillus Strain Against Mycobacterium Tuberculosis, Nature, London **155**: 300, 1945.
20. Smith, M. I., and Emmart, E. W.: The Action of Penicillium Extracts in Experimental Tuberculosis, Pub. Health Rep. **59**: 417-423, 1944.
21. Iland, C. N.: The Effect of Penicillin on the Tubercle Bacillus, J. Path. & Bact. **58**: 495-500, 1946.
22. Carr, L. G.: Action of Supernatants from Combined Growth of Fusarium Solani and Pseudomonas Aeruginosa Against the Tubercle Bacillus, U. S. Nav. M. Bull. **46**: 237-238, 1946.
23. Boissevain, C. H.: Growth Inhibition of Tubercle Bacilli by Fusarium sp., Proc. Soc. Exper. Biol. & Med. **63**: 555-556, 1946.
24. Arnstein, H. R. V.; Cook, A. H., and Lacey, M. S.: An Antibacterial Pigment from Fusarium Javanicum, Nature, London **157**: 333-334, 1946.
25. Miller, D. K., and Rekate, A. C.: Inhibition of Growth of Mycobacterium Tuberculosis by a Mold, Science **100**: 172-173, 1944.
26. Gerber, I. E., and Gross, M.: Inhibition of Growth of Mycobacterium Tuberculosis by a Mold Product, Science **101**: 616-617, 1945; **103**: 167-169, 1946.
27. Hollande, A. C.: Lyse massive den bacilles de Koch chez le Cobaye apres traitement a la clitocybine: Pouvoir inhibiteur de ce produit vis-a-vis du bacille typhique, de colibacille, de Brucella abortus, etc., Compt. rend. Acad. d. Sc. **221**: 361-363, 1945.
28. Ehrenberg, L.; Hedström, H.; Löfgren, L., and Tankman, B.: Antibiotic Effect of Agarics on Tubercle Bacilli, Svenska. kem. tidskr. **58**: 269-270, 1946; Svenska. farm. tidskr. **50**: 645-646, 1946.
29. Willstaedt, H., and Zetterberg, B.: Lactaroviolin, an Antibiotic Against the Tuberculosis Bacillus, Svensk. kem. tidsker. **58**: 306-307, 1946; Chem. Abstr. **41**: 2461, 1947.
30. Schiller, I.: Ueber erzwungene Antagonisten, Centralbl. f. Bakt. (Abt. I) **96**: 54-56, 1925; **103**: 304-314, 1927.
31. Barglowski, D.: Influences of Mycetes on Tubercle Bacilli, Am. Rev. Tuberc. **54**: 393-397, 1946.

tain few forms but is widely distributed among bacteria and other micro-organisms; some of these are capable of producing active antituberculosis agents.

In 1892 Rongali [32] demonstrated, for example, that a reciprocal antibiosis exists between various bacteria and Myco. tuberculosis. Nannotti and Prudden's results in this field have already been mentioned.

Ramond and Ravaut [33] established in 1899 that when various bacteria, such as B. subtilis, Staphylococcus albus, Staphylococcus aureus and Micrococcus tetragenus, are grown simultaneously with Myco. tuberculosis, the latter does not develop. When a drop of a culture of one of the preceding bacteria is added to a culture of the tubercle organism, growth of the latter is stopped. The metabolic products of the saprophytic bacteria had a similar, although weaker, effect on the growth of the parasite. In 1902 Michelazzi [34] reported that M. tetragenus has the capacity of suppressing Myco. tuberculosis not only in vitro but also in vivo. When the micrococcus was inoculated into experimental animals, the growth of the tubercle bacillus was prevented. The favorable effect of the administration of yeast on pulmonary tuberculosis was demonstrated by Huggard and Moreland in 1905.[35] The associative growth of Clostridium perfringens and Myco. tuberculosis was observed [36] to result in a lytic action of the former on the latter in vitro but not in vivo.

In 1912 Rappin [6] observed that culture filtrates of a number of spore-forming bacteria, such as B. subtilis, Bacillus mesentericus and Bacillus megatherium, have a suppressive effect on the development of the tubercle bacillus. When culture filtrates of the bacteria were injected into rabbits infected with the tubercle organism, the development of the disease was prevented and no toxic manifestations occurred. This activity was said to be due to the formation by the spore-forming bacteria of antibacterial agents designated as diastases. Thus the test tube experiments on the effect of bacterial products on the tubercle organism were confirmed by studies in experimental animals. Although these results were highly significant, they did not arouse sufficient interest and were not followed up immediately.

It took more than a decade before further studies on the antituberculosis properties of bacteria were reported. Most of the investigations were centered largely on the spore-forming aerobes. In 1926 Van Canneyt [37] demonstrated that B. subtilis exerts a lytic effect on Myco. tuberculosis. Olivier [38] also demonstrated that B. subtilis has the capacity of bringing about the lysis of the tubercle bacillus in eight to twelve days.

More recently, subtilin (obtained [39] from B. subtilis) was found to inhibit the growth of Myco. tuberculosis in Long's medium, in a dilution of 1:50,000; in 1:10,000, it was also bactericidal. This substance was also effective against experimental tuberculosis in guinea pigs. A strain of B. subtilis described as Bacillus licheniformis produced on a synthetic medium an agent which was active against the tubercle bacillus.[40] Other spore-forming bacteria, both aerobic [41] and anaerobic forms,[42] have now been found to cause the loss of virulence, to inhibit the growth of and even to bring about the lysis of tubercle bacilli. In some cases the culture filtrates of the antagonistic bacteria were as active as the culture itself. Some attempts have actually been made to utilize these culture filtrates in the treatment of human subjects.

Among the preparations obtained from spore-forming bacteria it may also be of interest to mention eumycin [43] and bacillin.[44] The latter was obtained from an organism isolated from soil enriched with tubercle bacilli.

Various non-spore-forming bacteria, including Escherichia coli and Pseudomonas aeruginosa are capable of exerting a pronounced tuberculostatic and tuberculocidal effect. Different strains of Esch. coli show great variations in their antibacterial action.[45] Throughout the most extensive literature on the antagonistic effects of Ps. aeruginosa and its antibiotic, pyocyanase, there are suggestions of their possible action on the tuberculosis organism. However, positive evidence has been submitted only recently. A twenty day culture of Ps. aeruginosa was found [46] to inhibit the growth of Myco. tuberculosis in dilutions of 1:80; a crude chloroform extract was effective in 1:128,000 dilution. Short exposure of the pathogen to the culture of the antagonist caused morphologic changes, followed by loss of acid-fastness and final lysis. An antibiotic substance designated as pyolipic acid was isolated from Ps. aeruginosa; this substance was characterized by decided antituberculosis properties.[47]

Certain streptococci have also been found to possess the capacity of producing antituberculosis substances. An organism described [48] as Micrococcus antibioticus was active against Myco. tuberculosis in vitro. Another coccus isolated by Mattick [49] from milk proved extremely effective against both human and bovine strains of the tubercle bacillus; this coccus yielded an antibiotic agent, nisin, which was active in a dilution of 0.000006.

This brief summary tends to establish the fact that bacteria also offer potential sources of antibiotics that possess tuberculostatic and tuberculocidal properties. Much is still to be done in this direction.

32. Rongali, D. B.: Sull'azione reciproca dei prodothi del bacillus tuberculosis di attri microorganismi patogeni e non-patogeni, Ann. d. Ist. d'ig. Sper. d. Univ. di Roma, 1892, vol. 2.

33. Ramond, F., and Ravaut, P.: Action des microbes sur le développement du bacille de la tuberculose, Arch. de Méd. expér. et d'anat. path. **11**: 494-497, 1899.

34. Michelazzi, A.: Intorno all' influenza del micrococco tetragono sul processo tuberculare del polmone, Riforma med. **4**: 158-163, 170-174, 182-185 and 194-197, 1902.

35. Huggard, W. R., and Morland, E. C.: The Action of Yeast in Tuberculosis and Its Influence on the Opsonic Index, Lancet **1**: 1493-1496, 1905.

36. Loris-Melikov, J., and Ostrovsky: Tuberculose et B. perfringens, Compt. rend. Soc. de biol. **74**: 227, 1913.

37. VanCanneyt, J.: Action du B. subtilis et de ses secretions sur le bacille de la tuberculose, Compt. rend. Soc. de Biol. **95**: 878-881, 1926.

38. Olivier, H. R.: Biological Properties of Bacillus Subtilis, Nature, London **157**: 238-239, 1946.

39. Salle, A. J., and Jann, G. I.: Subtilin—An Antibiotic Produced by Bacillus Subtilis: I. Action on Various Organisms, Proc. Soc. Exper. Biol. & Med. **60**: 60-64, 1945; J. Bact. **51**: 592, 1946.

40. Callow, R. K., and Hart, P. M.d'A.: Antibiotic Material from Bacillus Licheniformis (Weigmann, emend. Gibson) Active Against Species of Mycobacteria, Nature, London **157**: 334-335, 1946.

41. (*a*) Holst, E. C.: An Antibiotic from a Bee Pathogen, Science **102**: 593-594, 1945. (*b*) Puntoni, V., and Favia, N.: La Perte de la virulence du b. tuberculeux comme suite de son association avec le b. tuberculophile, Boll. d. sez. ital. d. Soc. internaz. di. microbiol. **6**: 158-160, 1934.

42. Passini, F.: Ueber die Lebensdauer der Tuberkelbazillen in Kulturen anaerober Fäulnissbakterien, Wien. klin. Wchnschr. **38**: 1182-1184, 1925; Centralbl. f. Bakt. **81**: 447, 1926.

43. Johnson, E. A., and Burdon, K. L.: Eumycin—A New Antibiotic Active Against Pathogenic Fungi and Higher Bacteria, Including Bacilli of Tuberculosis and Diphtheria, J. Bact. **51**: 591, 1946.

44. Foster, J. W., and Woodruff, H. B.: Bacillin, a New Antibiotic Substance from a Soil Isolate of Bacillus Subtilis, J. Bact. **51**: 363-369 and 371-380, 1946.

45. Peretz, L. H.; Newler, A. J., and Larionow, L. T.: Antagonistic Action of B. Coli on Tubercule and Diphtheria Bacteria, B. Proteus and B. Paracoli, Zhur. microbiol. epidemiol. immunol. **17**: 78-82, 1936.

46. Hughes, G. C., and Kierman, R. A.: A Product of Pseudomonas Aeruginosa Active in Vitro Against M. Tuberculosis, Nature, London **159**: 197, 1947.

47. Bergström, S.; Theorell, H., and Davide, H.: On a Metabolic Product of Ps. Pyocyanea, Pyolipic Acid, Active Against Mycobact. Tuberculosis, abstracted, Arch. Biochem. **10**: 165-166, 1946.

48. Dujardin-Beaumetz, E.: Action antibiotique exercée in vitro par certains Streptocoques et en particulier par un microcoque saprophyte, Compt. rend, Soc. de biol. **117**: 1178-1180, 1934.

49. (*a*) Mattick, A. T. R., and Hirsh, A.: A Powerful Inhibitory Substance Produced by Group N Streptococci, Nature, London **154**: 551, 1944; **155**: 797, 1945; Endeavour **5**: 24-28, 1946; (*b*) Sour Milk and the Tubercle Bacillus, Lancet **1**: 417-418, 1946; **2**: 5-8, 1947.

### PRODUCTION OF ANTITUBERCULOSIS AGENTS BY ACTINOMYCETES

Like the fungi and the bacteria, the actinomycetes comprise a number of organisms or species which produce antibiotics active against the tubercle bacillus. Some of the active agents that have so far been isolated or concentrated are actinomycin, litmocidin, nocardin, streptothricin and streptomycin. Of these, the last named is the most promising.

There are several significant points about the distribution of antimycobacterial properties among the actinomycetes: 1. A large number of species and strains of these organisms are capable of exerting an antituberculosis effect. 2. The active substances produced by these organisms vary greatly in their chemical properties and their toxicity to animals. 3. The action of these substances on mycobacteria and other micro-organisms vary greatly. Their antibiotic spectrums range from extremely narrow ones which are active only against certain mycobacteria, as in the case of the antismegmatis factor,[50] to exceedingly wide zones when the activity is broadly distributed against gram-positive and gram-negative bacteria and even against fungi, as in the case of streptothricin.[51]

Streptomycin possesses all the desirable properties as a potential chemotherapeutic agent in the treatment of tuberculosis. Two cultures of the organism producing streptomycin were isolated in September 1943; the announcement of the isolation of streptomycin itself was made in January 1944 in a paper by Schatz, Bugie and Waksman.[52] Soon afterward, Schatz and Waksman [53] reported that streptomycin is highly effective against Myco. tuberculosis and other mycobacteria. The human strain H 37 was particularly sensitive to this antibiotic. The tubercle organism, which was inhibited by only 0.2 microgram of the antibiotic, was six or more times more sensitive to streptomycin than was Esch. coli. Streptomycin possessed decided tuberculostatic and tuberculocidal properties; it was far more active than streptothricin, a closely related antibiotic. It was also active against various bacteria both in vitro and in vivo and had limited toxicity to experimental animals.[54] Not long afterward, Feldman and Hinshaw [55] established that streptomycin is effective in the treatment of experimental tuberculosis in guinea pigs. Evidence was thus obtained of the striking antibacterial activity of streptomycin in vivo. It resulted in the resolution, fibrosis or calcification of lesions in all animals and the apparent eradication of the infection in at least 30 per cent of the animals. Positive reactions to tuberculin tests have been reversed to negative reactions, free from the organism Myco. tuberculosis.

Different strains of the tubercle bacillus, freshly isolated from patients, were found by Youmans [56] to vary greatly in their sensitivity to streptomycin. The range in sensitivity was between 0.2 and 12.5 micrograms per cubic centimeter, although in the great majority of cases freshly isolated cultures were sensitive to less than 1 microgram per cubic centimeter. On contact with streptomycin, either in the test tube or in the human or animal body, Myco. tuberculosis gives rise to resistant strains which require far greater concentrations of the drug for their inhibition or destruction. When inoculated into animals, streptomycin-resistant cultures retained their resistance and no longer responded to streptomycin therapy.[57]

Actinomycetes produce other antibiotics which are active against Myco. tuberculosis. It is sufficient to mention nocardin, produced by Nocardia coeliaca.[58] This substance is found both in the culture medium and in the mycelium of the organism. It has an inhibiting effect on the slow-growing strains of Myco. tuberculosis varieties hominis and bovis in concentration of 10 to 50 per cent of the culture filtrate; unfortunately, it has only a slight in vivo effect.

The most important chemotherapeutic agent now known for tuberculosis, namely streptomycin, has been contributed by the actinomycetes. There is no doubt, however, that other agents supplementary or superior to streptomycin will be found, because of the wide occurrence of antimycobacterial substances among members of this group of micro-organisms. The possibility that different forms of streptomycin or even different sources of this antibiotic may vary quantitatively in their antituberculosis effect has also been indicated.[59]

### PRODUCTION OF ANTITUBERCULOSIS AGENTS BY HIGHER PLANTS

Finally, in order to make the survey complete, attention must also be directed to the higher, green plants which produce a variety of substances designated as "phytoncides" and which possess tuberculostatic and tuberculocidal properties. Marshak,[60] for example, obtained a crystalline preparation from the lichen Ramalina reticulata. This is a nonnitrogenous, water-insoluble substance; when it was administered subcutaneously in 10 to 20 microgram portions given once a day for a period of three weeks to guinea pigs that weighed from 350 to 400 Gm. there were no toxic effects. When the animals were infected intraperitoneally with human tubercle bacilli, strain H 37 RV, the antibiotic retarded the progress of the disease.

Other preparations derived from plants have been used at various times in the treatment of tuberculosis. It is sufficient to mention the alkaloid cepharanthine, used extensively in Japan, which is said to possess a limited toxicity and to exert a decided effect on experimental as well as clinical tuberculosis.[61]

### CHEMOTHERAPY OF TUBERCULOSIS FROM AN ANTIBIOTIC POINT OF VIEW

Although the results previously presented point to the production by micro-organisms of a large variety of substances that are active against the tubercle

50. Kelner, A., and Morton, H. E.: An Antibiotic (Anti-Smegmatis Factor) Produced by an Actinomycete, Specifically Inhibiting Species of Mycobacterium, Proc. Soc. Exper. Biol. & Med. **63**: 227-230, 1946.
51. Woodruff, H. B., and Foster, J. W.: In vitro Inhibition of Mycobacteria by Streptothricin, Proc. Soc. Exper. Biol. & Med. **57**: 88-89, 1944.
52. Schatz, A.; Bugie, E., and Waksman, S. A.: Streptomycin, a Substance Exhibiting Antibiotic Activity Against Gram-Positive and Gram-Negative Bacteria, Proc. Soc. Exper. Biol. & Med. **55**: 66-69, 1944.
53. Schatz, A., and Waksman, S. A.: Effect of Streptomycin and Other Antibiotic Substances upon Mycobacterium Tuberculosis and Related Organisms, Proc. Soc. Exper. Biol. & Med. **57**: 244-248, 1944.
54. Jones, D.; Metzger, H. J.; Schatz, A., and Waksman, S. A.: Control of Gram-Negative Bacteria in Experimental Animals by Streptomycin, Science **100**: 103-105, 1944.
55. Feldman, W. H., and Hinshaw, H. C.: Effects of Streptomycin on Experimental Tuberculosis in Guinea Pigs: A Preliminary Report, Proc. Staff. Meet., Mayo Clin. **19**: 593-599, 1944.
56. Youmans, G. P.: The Effect of Streptomycin in vitro on M. Tuberculosis Var. Hominis, Quart. Bull., Northwestern Univ. M. School. **19**: 207-209, 1945.
57. Karlson, A. G.; Feldman, W. H., and Hinshaw, H. C.: Persistence of Resistance of Tubercle Bacilli to Streptomycin During Passage Through Guinea Pigs, Proc. Soc. Exper. Biol. & Med. **64**: 6-7, 1947.
58. Emmart, E. W.: A Preliminary Report on a New Tuberculostatic Antibiotic from a Species of Nocardia, in Conference on Antibiotic Research, National Institute of Health, Washington, D. C., Jan. 31-Feb. 1, 1947.
59. Johnstone, D. B., and Waksman, S. A.: Streptomycin II. An Antibiotic Substance Produced by a New Species of Streptomyces, Proc. Soc. Exper. Biol. & Med. **65**: 294-295, 1947.
60. Marshak, A.: A Crystalline Antibacterial Substance from the Lichen Ramalina Reticulata, Pub. Health Rep. **62**: 3-19, 1947.
61. Junod, O.: La cépharantine: Médecine chimio-thérapique. Japonaise contre la tuberculose, Méd. et hyg. **4**: 1-2, 1946.

bacillus both in vitro and in vivo and thus offer promise as chemotherapeutic agents, streptomycin is the only one that has so far found practical application in the treatment of tuberculosis. Of a number of reports that have been submitted concerning the efficacy of streptomycin therapy in tuberculosis, only a few which have a direct bearing on the subject will be mentioned here.

To Feldman and Hinshaw [62] must go the credit for pioneering in these investigations. After being the first to demonstrate the effectiveness of streptomycin in experimental tuberculosis, they established by clinical investigations the chemotherapeutic potentialities of this drug. The criteria for a successful antituberculosis agent were summarized as follows: (*a*) the agent must be tolerated by the animal without producing irreversible physiologic derangements; (*b*) the progressive development of the disease must be reversed to nonprogressive, accompanied by resolution, fibrosis, and calcification; (*c*) the virulent infection must be eradicated, and (*d*) the effect must be produced in a reasonable time.

Clinically, streptomycin has been proved [63] to have a pronounced suppressive effect in miliary, laryngeal, meningitic, cutaneous, renal and exudative pulmonary tuberculosis. At first a small number of patients were treated, since only limited amounts and rather impure preparations of streptomycin were then available. Although the course of the disease was modified favorably and its progressive development suppressed, the result was believed to be associated with the bacteriostatic effect of the drug, and the lack of a rapid curative effect was ascribed to an insufficient bactericidal action.

As a result of treatment in the first 100 cases, Hinshaw, Feldman and Pfuetze considered themselves justified in coming to rather optimistic conclusions.[64] These can best be summarized in their own words:

> Streptomycin is an antibacterial agent which possesses the unique ability to inhibit the growth of Mycobacterium tuberculosis in vivo, both experimentally and clinically. The manifestations of tuberculosis may be suppressed both in experimental animals and in man, with at least temporary retardation of the pathologic processes as judged by objective criteria. In many instances streptomycin appears to suppress tuberculosis rather than to eradicate it, being apparently bacteriostatic rather than completely bactericidal in the concentrations which can be obtained in the tissues.

Tuberculous meningitis was definitely arrested by the use of streptomycin. Treatment consisted in the daily intrathecal administration, by lumbar or cisternal puncture, of 100 to 200 mg. of streptomycin for two to six weeks. In addition patients received by intramuscular injection 2 to 3 Gm. of the drug a day for six months. None of the patients who died in the first experiments had received intrathecal therapy, which frequently produced temporary clinical improvement that lasted only for several weeks or months.

Ulcerating tuberculous lesions of the respiratory passage, including the larynx, hypopharynx, trachea and large bronchi, have been treated in several instances, with prompt improvement of the patients in most cases; no recurrences occurred. In the prolonged treatment that is usually required for patients suffering from tuberculosis, there is the danger of an increase in resistance to the antibiotic, as was established for some of the patients. Although streptomycin did not exert a rapidly curative effect on clinical tuberculosis, it appeared to modify the course favorably by a suppressive effect on previously progressive tuberculosis.

In a discussion on the effects of streptomycin on pulmonary tuberculosis Bunn [65] has recently made the following observations: (*a*) The trend of the disease was reversed, as illustrated by the lack of spreads and exacerbations. (*b*) A majority of the patients were decidedly improved. (*c*) However, in no instance could the lesion be considered as cured. When a jury of sixteen disinterested specialists was allowed to examine the data submitted for their critical evaluation, a striking degree of agreement was obtained between the impressions of the participating investigators and those reported by the jury.

The other effects of streptomycin on the clinical course of tuberculosis were a lowering of the sedimentation rate, a dramatic reduction of fever in cases of hyperpyrexia, a pronounced gain in weight and subjective improvement. The production of sputum has usually been decidedly lessened and the cough has decreased in frequency and severity. Fourteen of a group of 47 patients gave negative sputum or gastric cultures after treatment with streptomycin.

In a group of 50 patients with miliary and/or meningeal tuberculosis who were treated with streptomycin, 50 per cent of the patients remained alive, although not all in perfect health, "but alive nevertheless, when by all previous standards, death should have taken place." Miliary lesions in the lungs have been observed by roentgen examination to disappear during the course of treatment. Total deafness occurred in 2 cases, and in 1 instance, complete depression of the bone marrow values; the latter was due to streptomycin, since its discontinuation was followed by a return of marrow function despite a progression of the miliary tuberculosis to death.

The conclusion was reached [65] that streptomycin is capable of healing certain tuberculous lesions and of serving as an adjuvant to existing forms of treatment in other types of tuberculosis. It was considered sufficiently toxic that its use must be accompanied by clinical observation and laboratory studies.

In another report on the treatment of tuberculosis with streptomycin [66] McDermott observed three significant phenomena in the majority of the tuberculous patients who received streptomycin: (*a*) a rapid, sometimes abrupt, fall in temperature and accompanying symptomatic improvement, not unlike the crisis observed in pneumococcus pneumonia; (*b*) a regression, and frequently a complete disappearance, of the pulmonary lesions demonstrable roentgenologically, and (*c*) the development of strains of tubercle bacilli which were resistant to the action of streptomycin in vitro. All three of these phenomena were most prominent in the more acutely ill patients of the hematogenous group.

In still another report [67] on the treatment of 4 children from 7 months to 3 years of age who had pul-

62. (*a*) Feldman, W. H.; Hinshaw, H. C., and Mann, F. C.: Streptomycin in Experimental Tuberculosis, Am. Rev. Tuberc. **52**: 269-298, 1945; (*b*) footnote 55.

63. (*a*) Hinshaw, H. C., and Feldman, W. H.: Streptomycin in Treatment of Clinical and Experimental Tuberculosis, Ann. New York Acad. Sc. **48**: 175-182, 1946. (*b*) Hinshaw, H. C.; Feldman, W. H., and Pfuetze, K. H.: Streptomycin in Treatment of Clinical Tuberculosis, Am. Rev. Tuberc. **54**: 191-203, 1946.

64. (*a*) Hinshaw, H. C.; Feldman, W. H., and Pfuetze, K. H.: Treatment of Tuberculosis with Streptomycin, J. A. M. A. **132**: 778-782 (Nov. 30) 1946; footnote 63b.

65. Bunn, P. A.: Streptomycin in the Treatment of Tuberculosis, in Conference of Antibiotics, Study Section, National Institute of Health, Washington, D. C., Febr. 1, 1947.

66. McDermott, W.; Muschenheim, C., and Bunn, P.: Streptomycin in the Treatment of Tuberculosis in Humans, in Conference of Antibiotics Study Section, National Institute of Health, Washington, D. C., Feb. 1, 1947.

67. Sanford, H. N., and O'Brien, D. E.: Streptomycin in Tuberculosis in Childhood: Results in Four Children, J. A. M. A. **133**: 691-693 (March 8) 1947.

monary tuberculosis, the daily administration of 1 Gm. of streptomycin for one month resulted in a definite improvement in the general condition of all 4 patients and regression of the appearance of pulmonary lesions.

### LOOKING AHEAD

The use of streptomycin in the treatment of tuberculosis presents certain challenging problems to the microbiologist, the chemist and the clinician. Most significant of these is the development by the tubercle organism of resistance to the streptomycin, and the drug's ineffectiveness against certain forms of tuberculosis.[68] In order to overcome these limitations an intensive search must be made for other agents that would be more effective alone or combined with streptomycin. The idea suggested by Smith and McClosky[69] of utilizing the possible synergistic effect of two agents, such as "promin" (sodium p,p'-diaminodiphenylsulfone-N,N'-didextrose sulfonate) and streptomycin, appears to offer certain promising possibilities. The combination of streptomycin with certain sulfones in the treatment of guinea pigs infected with experimental tuberculosis resulted in a greater therapeutic effect than the sum of the effects of the individual components.

A turning point has now been reached in the chemotherapy of tuberculosis. Although streptomycin may not be the final answer in the treatment of this scourge of mankind—and I hope that it is not—it has opened a new path, a path of antibiotic approach to chemotherapy, an approach sought since the discovery of the bacterial nature of the disease; the control of tuberculosis may finally materialize and thus advance man one step further in his battle against disease and epidemics.[70]

68. Youmans, G. P.; Williston, E. H.; Feldman, W. H., and Hinshaw, H. C.: Increase in Resistance of Tubercle Bacilli to Streptomycin: A Preliminary Report, Proc. Staff Meet., Mayo Clin. **21**: 126-127, 1946.

69. (*a*) Smith, M. I., and McClosky, W. T.: The Chemotherapeutic Action of Streptomycin and Promin in Experimental Tuberculosis, Pub. Health Rep. **60**: 1129-1138, 1945. (*b*) Smith, M. I.; McClosky, W. T.; Jackson, E. L., and Bauer, H.: Chemotherapeutic Action of Streptomycin and of Streptomycin with a Sulfone or Sulfadiazine on Tuberculosis, Proc. Soc. Exper. Biol. & Med. **64**: 261-269, 1947. (*c*) Soltys, M. A.: Antibiotic Action of Aspergillus Fumigatus Against Mycobacterium Tuberculosis, Nature, London **154**: 550-551, 1944.

70. In order to make the literature to this subject complete, certain other references are listed, although they are not cited in the text:

Bowser, B. M.: A Study of the Action of Certain Soil Bacteria on Mycobacterium Tuberculosis, Var. Hominis and Bovis, Thesis, University of Pittsburgh, 1942.

Bush, M. T.; Dickison, H. L.; Ward, C. B., and Avery, R. C.: Antibiotic Substances Active Against M. Tuberculosis, Federation Proc. **4**: 113, 1945; J. Pharmacol. & Exper. Therap. **85**: 237-246, 1945.

Cooke, R. E.; Dumphy, D. L., and Blake, F. G.: Streptomycin in Tuberculous Meningitis: Report of Its Use in One Year Old Infant, Yale J. Biol. & Med. **18**: 221-226, 1946.

Hart, P. M. d'A.: Chemotherapy of Tuberculosis, Brit. M. J. **2**: 805 and 849, 1946.

Dubos, R. J., and Davis, B. D.: Factors Affecting the Growth of Tubercle Bacilli in Liquid Media, J. Exper. Med. **83**: 409-423, 1946.

Emmart, E. W.: The Tuberculostatic Action of Streptothricin and Streptomycin with Special Reference to the Action of Streptomycin on the Chorioallantoic Membrane of the Chick Embryo, Pub. Health Rep. **60**: 1415-1421, 1945.

Krassilnikov, N. A., and Koreniako, A. I.: The Bactericidal Substance of the Actinomycetes, Mikrobiologiya **8**: 673-685, 1939.

Middlebrook, G., and Yegian, D.: Certain Effects of Streptomycin on Mycobacterium in Vitro, Am. Rev. Tuberc. **53**: 553-558, 1946.

Smith, D.: Quantitative Measurement of Growth of Mycobacterium Tuberculosis: Effect of Streptomycin, Proc. Soc. Exper. Biol. & Med. **64**: 36-40, 1947.

Smith, D., and Waksman, S. A.: Tuberculostatic and Tuberculocidal Properties of Streptomycin, J. Bact. **54**: 253-261, 1947.

Soparkar, M. B.: The Vitality of the Tubercle Bacillus Outside the Body, Indian J. M. Research **4**: 627-650, 1917.

Ungar, J., and Muggleton, J.: The Effect of Penicillin on the Growth of Human Type M. Tuberculosis, J. Path. & Bact. **58**: 501-504, 1946.

Waksman, S. A., and Woodruff, H. B.: Bacteriostatic and Bactericidal Substances Produced by a Soil Actinomyces, Proc. Soc. Exper. Biol. & Med. **45**: 609-614, 1940.

Waksman, S. A., and Woodruff, H. B.: Streptothricin, a New Selective Bacteriostatic and Bactericidal Agent, Particularly Active Against Gram-Negative Bacteria, Proc. Soc. Exper. Biol. & Med. **49**: 207-210, 1942.

Williams, R. S., and Hoy, W. A.: The Viability of B. Tuberculosis (Bovinus) on Pasture Land, in Stored Faeces and in Liquid Manure, J. Hyg. **30**: 413-419, 1930.

Wolinsky, E., and Steenken, W., Jr.: Effect of Streptomycin on the Tubercle Bacillus, Am. Rev. Tuberc. **55**: 281-228, 1947.

The complete literature on the use of streptomycin in experimental and clinical tuberculosis cannot be presented for the simple reason that many of these papers are only now in the process of publication.

# CARCINOMA OF THE ESOPHAGUS AND THE CARDIAC END OF THE STOMACH

## Immediate and Late Results of Treatment by Resection and Primary Esophagogastric Anastomosis

RICHARD H. SWEET, M.D.
Boston

Until 1938 when Phemister and his associates[1] performed the first successful transthoracic resection for carcinoma of the lower end of the esophagus invading the cardia, the prospect of treatment of this disease was dismal if not hopeless. In the majority of cases in which the tumor involved the midthoracic segment, the application of the Torek procedure[2] resulted in disappointment because of the failure of this operation to provide satisfactory palliation and its inefficacy as a method of controlling the disease.[3]

As a result of several years of experience with resection and primary anastomosis within the thorax, the entire situation has changed, and the immediate and late results of treatment by resection and primary esophagogastric anastomosis may be evaluated. The elimination of the distressing dysphagia provided by this operation has been most gratifying, and the fact that a recurrence of the tumor at the site of anastomosis is exceedingly unusual insures the best palliation available for patients afflicted with this terrible disease. With regard to the possibility of cure, although more time will be required to accumulate a large series of cases in which the operation was performed long enough ago to observe survival periods of three years or longer, it is already apparent that the three to five year survival rate will ultimately approximate that of carcinoma located in other internal viscera.

The first transthoracic resection for carcinoma of the cardia to be performed at the Massachusetts General Hospital was in 1939. From then until Jan. 1, 1947, 213 patients with carcinoma of the esophagus or cardiac end of the stomach have been operated on. Resections were performed in 141 cases. Ninety-one of these consisted in transthoracic partial gastrectomy and esophagectomy followed by primary intrathoracic esophagogastric anastomosis. These cases included 27 epidermoid lesions arising in the lower fourth of the esophagus and 64 adenocarcinomas arising from intraesophageal gastric mucosa or from the stomach itself and invading the cardia. Although an appreciable number of patients with carcinoma in the midthoracic segment of the esophagus had already been treated by resection and high intrathoracic esophagogastric anastomosis just below the aortic arch, the first patient at the Massachusetts General Hospital in whom the esophagus was pulled up from beneath the aortic arch for the performance of a supra-aortic anastomosis was treated in May

From the surgical services of the Massachusetts General Hospital.

Read before the Section on Surgery, General and Abdominal, at the Ninety-Sixth Annual Session of the American Medical Association, Atlantic City, N. J., June 11, 1947.

1. Adams, W. E., and Phemister, D. B.: Carcinoma of the Lower Thoracic Esophagus: Report of Successful Resection and Esophagogastrostomy, J. Thoracic Surg. **7**: 621, 1938.

2. Torek, F.: First Successful Resection of Thoracic Portion of Esophagus for Carcinoma: Preliminary Report, J. A. M. A. **60**: 1533 (May 17) 1913.

3. (*a*) Sweet, R. H.: Surgical Management of Carcinoma of the Midthoracic Esophagus, New England J. Med. **233**: 1, 1945; (*b*) Carcinoma of the Midthoracic Esophagus: Its Treatment by Radical Resection and High Intrathoracic Esophagogastric Anastomosis, Ann. Surg. **124**: 653, 1946.

1944. Since that time 50 patients with carcinoma of the midthoracic segment have been treated by resection and high anastomosis. Twenty-one of these had an anastomosis just below the aortic arch, and in 29 the anastomosis was performed above the arch, frequently just below the dome of the left pleural cavity. These

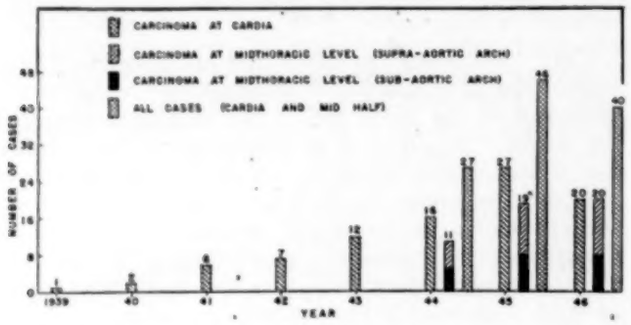



Chart 1.—Numbers and types of cases as they have occurred from year to year.

50 cases were all epidermoid carcinoma histologically. Chart 1 serves to illustrate the numbers and types of cases as they have occurred from year to year.

## RESECTION AND PRIMARY ESOPHAGOGASTRIC ANASTOMOSIS

*Technic of Operation.*—No important changes have been made in the technic of resection and primary esophagogastric anastomosis used in each type of case since previous reports were made.[4] A description of the technical aspects will therefore be omitted.

*Preoperative and Postoperative Care.*—Little change has been made in the preparation and postoperative care of these patients since previous reports.[4a] The most important development has been the routine use of penicillin and more recently of streptomycin for the prevention of infection. The use of these antibiotics has almost eliminated the element of sepsis, which was formerly the most frequent cause of postoperative complications and the principal cause of death in the immediate postoperative period.

Other changes such as elimination of the continuous use of the inlying Levin tube, earlier ambulation, more frequent application of the operation of ligation of the superficial femoral veins to prevent pulmonary embolism and earlier administration of oral feedings are features of minor importance.

In recent months all patients have been given the benefit of consultation with a cardiologist,[5] who has taken a serious interest in the possibility of reducing the occurrence of cardiac complications. Since the problem of infection is now under better control, such complications have caused the most frequent and the most serious difficulty. The routine use of a low sodium diet to diminish the possibility of the development of acute pulmonary edema and the preoperative and postoperative administration of quinidine sulfate in an effort to prevent the occurrence of cardiac arrhythmias appear to have been highly beneficial, although a larger experience will be necessary before accurate conclusions may be drawn.

4. (*a*) Sweet, R. H.: Transthoracic Gastrectomy and Esophagectomy for Carcinoma of the Stomach and Esophagus, Clinics **3**: 1288, 1945; (*b*) footnote 3b.

5. Dr. E. B. Bland, physician at the Massachusetts General Hospital, assisted in the management of the cardiac problems in these cases.

## SURGICAL EXPERIENCE WITH TWO HUNDRED AND THIRTEEN CASES OF CARCINOMA OF THE THORACIC ESOPHAGUS AND CARDIAC END OF THE STOMACH

*Selection of Cases for Surgical Intervention.*—No patient was refused the benefit of surgical treatment because of age alone. In general, if the condition of the patient seemed good enough to offer reasonable prospect of his survival, an exploratory operation was performed. Obvious evidences of incurability such as the presence of distant metastases or involvement of the liver were taken as contraindications. In carcinoma of the thoracic segment of the esophagus a persistent fever or an intense boring pain in the back, both indicative of deep ulceration and infection, usually indicate that the condition is inoperable, and an operation was not performed in the majority of such cases. A further contraindication in the case of midthoracic lesions is bronchoscopic evidence of invasion of or fixation to the trachea or bronchi.

*Resectability.*—Of all the cases of carcinoma of the thoracic segment of the esophagus and cardiac end of the stomach which were observed from 1939 to January 1947, 213 were considered to be suitable for operative intervention. Chart 2 summarizes in graphic form the results of treatment in the entire series. Seventy-two lesions were hopeless from the point of view of removal and a resection was not performed. In 141 cases, however, it was possible to remove the growth and perform an esophagogastric anastomosis. Thus the resectability rate of the entire group of 213 cases was 66.2 per cent. A subdivision of the cases according to the level of occurrence of the tumor reveals that there was no significant difference between the low and the high cases with regard to resectability. Of 72 cases of carcinoma involving the midthoracic segment of the esophagus, 22 were inoperable; but a resection was performed in 50 cases, a resectability rate of 69.4 per cent. Furthermore, of the 141 cases of carcinoma of the cardia and lower part of the esophagus, 50 were not resectable and a resection was performed in 91 cases, a resectability rate of 64.5 per cent (table 1).

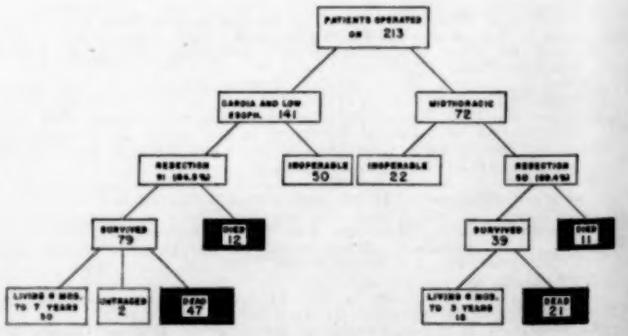



Chart 2.—Summary of results of exploratory operations or resection and primary esophagogastric anastomosis for carcinoma of the esophagus and cardiac end of the stomach. (This does not include 14 cases of carcinoma of the midthoracic esophagus treated by the Torek operation and reported previously.[4b])

*Immediate Results of Operation.*—Occurrence Rate of Complications and Operative Mortality: Table 2 demonstrates the immediate results of operation and the occurrence rate of complication and operative mortality. Of the 141 patients treated by radical resection and primary anastomosis 93 (66 per cent) made an

uncomplicated recovery. Twenty-five other patients (17.7 per cent) in whom complications developed made an ultimate recovery, and 23 (16.3 per cent) died as a result of complications during the early postoperative period.

Because of the considerably greater magnitude and seriousness of this operative procedure when it is applied to cases in which the growth lies in the midthoracic segment, as compared to that for lesions at the cardia, it is important to differentiate between the two groups, as will be apparent from a further consideration of the data presented in table 2. Thus of the 91 cases of carcinoma at the cardia, which requires a less serious operation than that necessary for the midthoracic group of lesions, 62 (68 per cent) resulted in an uncomplicated recovery. The recovery, though complete, was attended by complications in 17 cases (18.7 per cent) and in 12 cases (13.2 per cent) the complications resulted in death. In contrast to this, of the 50 cases of operation for carcinoma in the midthoracic segment of the esophagus, 31 (62 per cent) resulted in an uneventful recovery. In 8 cases (16 per cent) the convalescence was attended by complications but the patient recovered. In 11 cases (22 per cent), however, the complications were of such severity that the patient died.

TABLE 1.—*Resectability Rate in All Cases of Carcinoma of the Esophagus and Cardia Chosen for Surgical Intervention*

| Location | Total Cases | Exploration Only | Resection | Resectability, % |
|---|---|---|---|---|
| Carcinoma of the midthoracic esophagus | 72 | 22 | 50 | 69.4 |
| Carcinoma of the cardia and lower esophagus | 141 | 50 | 91 | 64.5 |
| Total | 213 | 72 | 141 | 66.2 |

Further analysis of the complication and mortality rates occurring in cases of operation for carcinoma located in the midthoracic segment of the esophagus reveals that the incidence of complications and the frequency of postoperative mortality is considerably greater in those cases in which a supra-aortic arch anastomosis is required than in those in which the anastomosis can be performed just below the arch. There were 21 cases of anastomosis just beneath the aortic arch, in 15 (71 per cent) of which the patient made an uncomplicated recovery; in 2 cases (9.5 per cent) complications developed but the patient recovered, and 4 patients (19 per cent) died as a result of postoperative complications. On the other hand, of the 29 cases of supra-aortic arch anastomosis only 16 (55 per cent) resulted in an uncomplicated recovery; in 6 patients (21 per cent) there developed complications, although they recovered, and 7 patients (24 per cent) died of complications. These data are presented in table 3.

### ANALYSIS OF THE COMPLICATIONS OCCURRING AFTER RESECTION

*Principal Complications.*—Table 4 gives a list of the principal complications after resection which were recognized either clinically or as a result of postmortem examination. They are arranged according to the location of the lesion and the type of operation which was performed and include all complications previously reported[6] in addition to those which have occurred in the cases which have been added since those reports were made. It is important to emphasize once again the fact that in some cases two or more complications were observed, so that the sum of all complications is greater than the total number of complicated cases.

TABLE 2.—*Complications and Mortality Rate in All Patients with Carcinoma of the Esophagus and Cardia Treated by Resection with Esophagogastric Anastomosis*

| Type of Operation | No. of Patients | Recovery: Uncomplicated | Recovery: Complicated | Deaths | Mortality, % |
|---|---|---|---|---|---|
| Esophagectomy for carcinoma of midthoracic esophagus | 50 | 31 | 8 | 11 | 22.0 |
| Partial gastrectomy and esophagectomy for carcinoma invading the cardia | 91 | 62 | 17 | 12 | 13.2 |
| Total | 141 | 93 | 25 | 23 | 16.3 |

*Manifestations of Infection.*—There has been a relative decrease in the number of infections which have occurred since penicillin has become available for routine use, with almost complete disappearance in the low and infra-aortic anastomosis groups. Sepsis is still a factor to be reckoned with, however, in the supra-aortic anastomosis group. In 3 of this group of cases empyema developed. In 2 instances a small pocket of pus developed in the superior aspect of the chest; these were recognized only at autopsy. In 1 case (to be described later) the infection resulted from a leakage at the suture line and was a part of the widespread sepsis which was the cause of the patient's death. In the other the empyema was an insignificant observation in a patient who died of cardiac failure. In the third case there developed bilateral basal empyema accumulations, which were drained successfully by bilateral resection of ribs.

*Mediastinitis.*—Only 1 case of mediastinitis was observed in addition to those reported previously. This occurred in the patient in whom sepsis developed as a result of leakage at the anastomosis.

TABLE 3.—*Carcinoma of the Midthoracic Esophagus: Complication and Mortality Rates According to the Type of Operation*

| Type of Operation | No. of Patients | Recovery: Uncomplicated | Recovery: Complicated | Deaths | Mortality, % |
|---|---|---|---|---|---|
| Esophagectomy with anastomosis below the aortic arch | 21 | 15 | 2 | 4 | 19.0 |
| Esophagectomy with anastomosis above the aortic arch | 29 | 16 | 6 | 7 | 24.1 |
| Total | 50 | 31 | 8 | 11 | 22.0 |

*Cardiac Disorders.*—Since the relative decrease in the occurrence of complications which result from infection and as a result of the greater use of the supra-aortic type of anastomosis for high growths in the midthoracic

6. (*a*) Sweet, R. H.: Transthoracic Resection of the Esophagus and Stomach for Carcinoma: Analysis of the Postoperative Complications; Causes of Death, and Late Results of Operation, Ann. Surg. **121**: 272, 1945; (*b*) footnote 3b.

segment of the esophagus, cardiac disorders have come to occupy the place of greatest numeric importance in the list of complications after resection. The relatively larger number of cases of myocardial infarction, congestive failure and cardiac arrhythmia which were observed in the patients who had carcinoma of the midthoracic esophagus as compared with those whose growth was at the cardia is obvious from table 4. This is especially true of those in whom it was necessary to dissect the growth out from beneath the aortic arch for the performance of a supra-aortic arch anastomosis. In 91 cases of low intrathoracic anastomosis there were 15 cardiac complications (16 per cent). In the 21 cases of high subaortic arch anastomosis there were 6 such complications (28 per cent), and in the 29 cases of supra-aortic arch anastomosis there were 12 cardiac complications (41 per cent). This difference is not

TABLE 4.—*Complications Following Resection (Arranged According to Type of Operation)*

| | Carcinoma at Cardia (Low Intrathoracic Anastomosis) | Carcinoma of Midthoracic Esophagus | | Total |
|---|---|---|---|---|
| | | Infra-aortic Anastomosis | Supra-aortic Anastomosis | |
| No. of patients operated on... | 91 | 21 | 29 | 141 |
| Infection | | | | |
| Empyema | 3 | 1 | 3 | 7 |
| Mediastinitis | 3 | 0 | 1 | 4 |
| Wound sepsis | 1 | 0 | 1 | 2 |
| Cardiac disorders | | | | |
| Myocardial infarction | 2 | 1 | 2 | 5 |
| Congestive failure | 6 | 2 | 6 | 14 |
| Auricular flutter | 2 | 0 | 1 | 3 |
| Auricular fibrillation | 5 | 3 | 3 | 11 |
| Pulmonary complications | | | | |
| Embolism | 2 | 1 | 0 | 3 |
| Pneumonia | 2 | 1 | 1 | 4 |
| Atelectasis | 2 | 1 | 1 | 4 |
| Vascular disorders | | | | |
| Thrombosis of splenic vein | 1 | 0 | 0 | 1 |
| Thrombophlebitis of leg veins | 4 | 0 | 0 | 4 |
| Miscellaneous | | | | |
| Uremia | 0 | 0 | 1 | 1 |
| Chylous hydrothorax | 0 | 0 | 2 | 2 |
| Acute parotitis | 2 | 0 | 0 | 2 |
| Leakage from anastomosis | 1 | 0 | 1 | 2 |
| Surgical shock | 0 | 0 | 1 | 1 |

unanticipated in view of the fact that the higher the tumor lies, the more extensive the dissection necessary in the mediastinum; moreover, the duration of the operative procedure is considerably prolonged.

*Pulmonary Complications.*—Pulmonary complications have been observed at about the same rate as previously reported. Two additional cases of pulmonary embolism have been observed. This makes 3 cases in 141 operations, an incidence which is rather high but not inconsistent with the advanced age and poor general condition of the majority of these patients.

*Vascular Disorders.*—Included among vascular disorders are a case of thrombosis of the splenic vein discovered at autopsy and 4 cases of thrombophlebitis of the veins of the leg. The latter were treated by ligation and interruption of the superficial femoral veins.

*Miscellaneous Complications.*—Miscellaneous complications include 1 case of uremia, 2 of chylous hydrothorax (previously reported [3b]), 2 of acute parotitis, 1 of transitory surgical shock and 2 of leakage from the anastomosis. One case of leakage occurred in an elderly man who had a resection for carcinoma of the cardia with a low intrathoracic anastomosis. It was characterized by the the transitory discharge of gastric contents through the intercostal drainage sinus. Spontaneous closure took place after a few days. In the second case the leakage was the cause of the patient's death. It resulted from technical difficulties in the performance of a supra-aortic arch anastomosis in an elderly woman who had an anomalous right innominate artery which arose from the aortic arch at its junction with the descending aorta. The presence of this large vessel at the place where the proximal segment of the esophagus had to be pulled out from beneath the aortic arch made it practically impossible to perform a satisfactory anastomosis, and leakage occurred.

TABLE 5.—*Causes of Death After Resection (Arranged According to Type of Operation)*

| | Carcinoma at Cardia (Low Intrathoracic Anastomosis) | Carcinoma of Midthoracic Esophagus | | Total |
|---|---|---|---|---|
| | | Infra-aortic Anastomosis | Supra-aortic Anastomosis | |
| Sepsis | 4 | 0 | 1 | 5 |
| Cardiac disorders | | | | |
| Congestive failure | 5 | 1 | 3 | 9 |
| Myocardial infarction | 1 | 1 | 0 | 2 |
| Pulmonary disorders | | | | |
| Pneumonia | 0 | 1 | 0 | 1 |
| Embolism | 1 | 0 | 0 | 1 |
| Atelectasis | 0 | 1 | 0 | 1 |
| Miscellaneous | | | | |
| Chylous hydrothorax | 0 | 0 | 2 | 2 |
| Infarction of liver | 1 | 0 | 0 | 1 |
| Uremia | 0 | 0 | 1 | 1 |
| Total | 12 | 4 | 7 | 23 |

TABLE 6.—*Survival After Transthoracic Partial Gastrectomy for Carcinoma of the Lower Part of the Esophagus or Cardia*

| | 1939 | 1940 | 1941 | 1942 | 1943 | 1944 | 1945 | 1946 | Total | |
|---|---|---|---|---|---|---|---|---|---|---|
| Total number of operations | 1 | 2 | 6 | 7 | 14 | 16 | 29 | 16 | 91 | % of Those Who Survived a Given Time |
| Hospital deaths | 0 | 0 | 1 | 4 | 2 | 1 | 3 | 1 | 12 | |
| Total analyzed | 1 | 2 | 5 | 3 | 12 | 15 | 26 | 15 | 79 | |
| Survivals | | | | | | | | | | |
| 6 months | 1 | 2 | 5 | 3 | 10 | 12 | 21 | 11 | 65 | 82.0 |
| 12 months | 1 | 1 | 4 | 2 | 8 | 7 | 15 | .. | 38 | 48.0 |
| 18 months | 1 | 1 | 3 | 2 | 7 | 5 | 9 | .. | 28 | 44.0 |
| 2 years | 1 | 0 | 2 | 2 | 5 | 2 | .. | .. | 12 | 31.5 |
| 3 years | 1 | 0 | 2 | 2 | 4 | .. | .. | .. | 9 | 39.0 |
| 4 years | 1 | 0 | 2 | 2 | .. | .. | .. | .. | 5 | 45.5 |
| 5 years | 1 | 0 | 2 | .. | .. | .. | .. | .. | 3 | 37.5 |
| 6 years | 1 | 0 | .. | .. | .. | .. | .. | .. | 1 | 33.3 |
| 7 years | 1 | .. | .. | .. | .. | .. | .. | .. | 1 | 100.0 |

Note: Thirty patients were operated on three or more years ago. Seven died immediately postoperatively. Of the remaining 23, 9 are living and apparently well at the end of three years, making a three year survival rate of 39 per cent.

## CAUSES OF DEATH AFTER OPERATION

Table 5 lists the causes of death which occurred during the early postoperative period, arranged according to the type of operation performed. The most frequent

single cause of death was congestive failure of the heart, which accounted for 9 of the 23 fatalities The relative importance of this cause among the cases of high midthoracic carcinoma with supra-aortic anastomosis is manifest. The next most frequent cause of death was sepsis, which occurred in 5 cases. In the remainder of the cases the causes were distributed widely, as follows: pulmonary embolism 1; pneumonia 1; massive pulmonary atelectasis 1; chylous hydrothorax 2; infarction of the liver 1; uremia 1, and myocardial infarction 2.

### LATE RESULTS OF RESECTION

Enough time has now elapsed since the performance of the operation in many of the cases that a two year or longer period of observation is possible. Of the 141 patients on whom a resection was performed, 23 died in the hospital. The records of the 118 survivors are available for study. A successful follow-up study has been made in 116 of these cases. Two patients remain untraced and for the purpose of this study are considered as dead as of the last date on which they were known to be living.

TABLE 7.—*Survival After Resection of Carcinoma of the Midthoracic Esophagus*

| | 1944 | 1945 | 1946 | Total | % of Those Who Had the Opportunity to Survive a Given Time |
|---|---|---|---|---|---|
| Total no. of operations | 12 | 19 | 19 | 50 | |
| Hospital deaths | 4 | 3 | 4 | 11 | |
| Total analyzed | 8 | 16 | 15 | 39 | |
| Survivals | | | | | |
| 6 months | 6 | 11 | 13 | 30 | 77.0 |
| 12 months | 4 | 8 | .. | 12 | 50.0 |
| 18 months | 3 | 2 | .. | 5 | 31.0 |
| 24 months | 3 | .. | .. | 3 | 37.5 |

Although the ultimate results will probably be similar, it is desirable at the present time to separate the cases of carcinoma of the midthoracic segment from those at the cardia because there are so few of the former group of cases in which the results of operation have been observed longer than two years and none longer than three years.

### SURVIVAL FOLLOWING RESECTION FOR CARCINOMA OF THE LOWER ESOPHAGUS AND CARDIAC END OF THE STOMACH

Table 6 outlines the facts regarding the survival of 91 patients operated on for carcinoma of the lower part of the esophagus and cardia. For each year, beginning with 1939 and ending with 1946, are shown the total number of patients operated on, the number of deaths in the hospital, the total survivors per year and the number of patients alive at given periods of time after operation, starting with six months and ending with the number of years which have elapsed between the year the operations were performed and the last day of 1946.

A study of this table reveals that the majority of fatalities from metastases or recurrence of the disease occur during the first two years after operation. It will be seen also that an appreciable number of patients have survived for more than two years. The three year survival rate in this series is particularly interesting. The table shows that there were 30 patients whose operation was performed three or more years ago. Seven of these patients died as a result of operation, leaving 23 who had an opportunity to survive. Nine of these 23 patients were alive three or more years after operation. This represents a three year survival rate of 39 per cent. A further inspection of the table reveals that

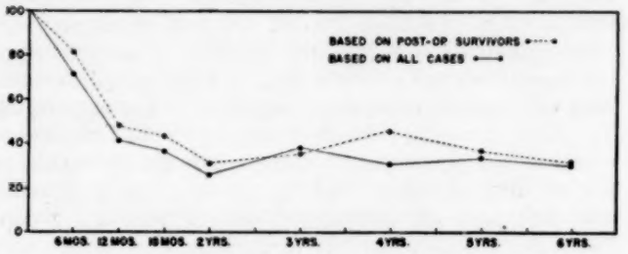



Chart 3.—Graphic representation of yearly survival rate (the per cent of those who had the opportunity to survive a given period) following resection and esophagogastric anastomosis in 91 cases of carcinoma of the cardia. Seventy-nine patients survived the operation.

of these 9 patients 4 are alive three years, 2 four years, 2 five years and 1 seven years after surgical intervention.

A graphic representation of the percentage survival each year is shown in chart 3. One line on this chart shows the percentages of survivors following resection excluding the patients who died in the hospital immediately after the operation. For the sake of comparison, another line gives the percentages of survivors based on the entire series of patients undergoing operation, not excluding the postoperative fatalities.

These results give reason for considerable encouragement. They suggest that as with carcinoma in other organs of the body, the majority of deaths from recurrence and metastasis after resection of carcinoma of the esophagus and cardia occur during the first two years after the operation. Furthermore, if the patient survives three years his chances of further survival and possibly of cure are reasonably good (chart 3, table 6). Such a result has not been obtained by any other method of treatment of this disease.

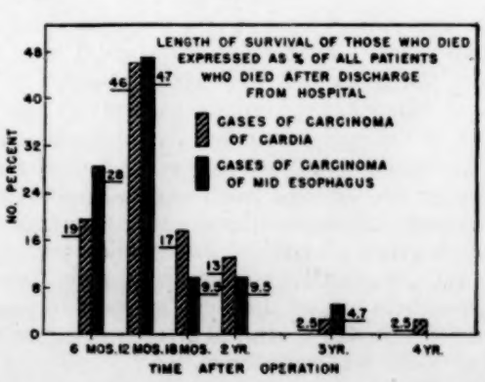



Chart 4.—Duration of life among those patients who died following discharge from the hospital.

### SURVIVAL FOLLOWING RESECTION OF CARCINOMA OF THE MIDTHORACIC ESOPHAGUS

Holmes and Schulz [7] have shown that no patient with carcinoma of the esophagus treated by supervoltage roentgen radiation survived longer than two years. This is not much different from the survival figures of

7. Holmes, G. W., and Schulz, M. D.: Supervoltage Radiation: A Review of the Cases Treated During an Eight Year Period (1937-1944), Am. J. Roentgenol. **55**: 533, 1946.

Nathanson and Welch,[8] who have indicated that in untreated cases almost all patients are dead less than two years after the onset of the first symptoms.

In the study of the late results of resection in cases of carcinoma of the midthoracic esophagus, it must be remembered that the first patient in this group was treated in 1944. Although not enough time has elapsed, therefore, to make studies of the end result in this group particularly significant, table 7 serves to reveal the same tendencies as are seen in table 6, which deals with carcinoma of the lower segment of the esophagus. The large number of deaths occurring in the first twelve months is apparent, and the percentage survivals at six months, one year, eighteen months and two years after operation are similar to those of the other group. Subsequent reports will be made regarding these cases after sufficient time has elapsed.

### VALUE OF THE OPERATION IN THE PALLIATION OF THE DISEASE

In carcinoma of the esophagus the most distressing symptom is dysphagia. The misery attendant on the almost complete obstruction which ultimately afflicts patients who have the disease is pathetic to observe. Any method of treatment which will alleviate this distressing symptom is gratefully received. Bougienage and roentgen radiation are notoriously ineffectual except to afford transitory periods of relief in a few cases. It has been a gratifying observation that even in those who die of recurrent or metastatic disease following resection with esophagogastric anastomosis there seldom develops a recurrence at the anastomotic stoma. This fact alone makes the operation worth while if the patient can thus be kept comfortable for a period of at least six months to one year.

The duration of palliation obtained by the use of this surgical procedure in cases of carcinoma of the esophagus and cardia varied from six months to four years. In the group of cases of carcinoma of the cardia, of the 46 patients who died subsequent to the operation 9 lived six months or less, 21 lived six months to one year, 8 lived twelve to eighteen months, 6 lived two years, 1 lived three years and 1 lived four years. In the group of cases of carcinoma of the midthoracic segment of the esophagus, of those who died subsequent to the operation 6 lived six months or less, 10 lived from six months to one year, 2 lived twelve to eighteen months, 2 lived two years and 1 lived three years. Chart 4 illustrates the relative length of survival in each group of cases of those patients who died subsequent to their discharge from the hospital. Because the total numbers are so different in the two groups, the length of survival is shown in each category as a percentage of the total number of deaths in that group.

As a method of palliation alone, therefore, resection and anastomosis has been proved superior to any other form of treatment yet available in the management of carcinoma of the esophagus and cardiac end of the stomach. The significant fact, however, is that many patients survive longer than a year; in some the relief from dysphagia produced by resection and esophagogastric anastomosis has been prolonged for two years or more.

8. Nathanson, I. T., and Welch, C. E.: Life Expectancy and Incidence of Malignant Disease, Am. J. Cancer **28**: 40, 1936.

## ABSTRACT OF DISCUSSION

Dr. Dallas B. Phemister, Chicago: Dr. Sweet is to be congratulated on the superb operative results and on the excellent studies that he has made on the patients. The encouraging aspect of this field of surgical practice is the rapid decline in operative mortality and the extension of the field of operability to include high lesions in the esophagus and advanced lesions of the stomach, sometimes adherent to surrounding structures which must also be excised.

At first the mortality was extremely high both in Japan, where resection by thoracolaparotomy was first performed, and in this country, where transthoracic resection was first done successfully. The mortality has so declined that in experienced hands it now ranges around 15 per cent. In the last 26 operations that Dr. Adams and I have performed there were but 2 operative deaths. A discouraging aspect is that the incidence of recurrence after operation has not improved to the same extent that the operative mortality has been reduced. The frequency of recurrence varies with the location of the tumor. The most favorable location is in the lower end of the esophagus. Tumors of the esophagus narrow the lumen and produce obstructive symptoms relatively early, from which the diagnosis is sooner or later made. Metastases are commonly present by the time the patient receives operative treatment. The early metastases from carcinoma of the lower esophagus are usually located in the lymph nodes along the upper part of the lesser curvature of the stomach which are removable. This makes for a better prognosis in carcinoma of the lower esophagus. Dr. Sweet referred to the first successful one stage transthoracic resection and anastomosis, done by Dr. Adams and myself. The tumor was in this location and lymph node metastases in the lesser curvature of the stomach were removed. The patient is now well nine and one-half years after operation. Recurrence is more frequent after operation for carcinoma of the upper part of the esophagus because the neoplastic growth invades surrounding structures and metastasizes to regional lymph nodes that are difficult or impossible to remove. Carcinoma of the proximal stomach usually begins at a distance from the esophageal opening and may grow silently for as long as nine to eighteen months before it finally reaches the esophagus, produces obstructive symptoms and gets diagnosed. By that time it has often spread to surrounding structures and metastasized to regional lymph nodes, which makes for a high incidence of recurrence after resection. Early diagnosis and early surgical operation are the keynotes for future improvement.

Dr. Morris T. Friedell, Chicago: What portion of the vagus nerves is resected in Dr. Sweet's operation, and does this result in any disturbance of gastric motility?

Dr. Richard H. Sweet, Boston: The work of Dr. Phemister has always been a great stimulus to me. In this transthoracic operation, extremely long sections of the vagus nerve are resected, and I have come to disregard the vagus nerve so thoroughly in dealing with these carcinomas of the esophagus that I pay little attention to it. The nerve is usually divided just below the aortic arch, often above the pulmonary branches. It is not divided above the origin of the recurrent nerve, however. I would like to comment on something which causes concern to the thoracic surgeon, namely, that I have never been aware of any vago-vagal reflex in man while handling the vagus nerve during these operations. The motility of the stomach is of course interfered with, and yet there is something peculiar about that observation, because the roentgenologists at Massachusetts General Hospital have commented without any prompting whatever that the lack of gastric motility, about which the surgeon used to be so concerned, seems to be less and less obvious as time goes on. Why that should be, I do not know, except that the amount of dissection which I now do toward the antrum and the duodenal end is much greater than it used to be.

# STREPTOMYCIN IN OCULAR INFECTIONS

JOHN G. BELLOWS, M.D.
and
CHESTER J. FARMER
Chicago

The adoption of streptomycin for the treatment of various infections caused by organisms either insensitive or resistant to sulfonamide compounds and penicillin has aroused much interest among ophthalmologists. Streptomycin has been shown by in vitro and in vivo experiments to be bacteriostatic against certain gram-positive organisms as well as against a wide variety of hitherto resistant gram-negative forms.

The literature on the use of streptomycin in ocular infections is extremely meager. Owens [1] reported 1 case of a severe corneal infection caused by Escherichia coli, which responded satisfactorily to the local application of streptomycin. Alberstadt and Price [2] treated 9 patients with corneal infections with streptomycin applied locally. In spite of the fact that adequate bacteriologic data were unobtainable, they concluded that the addition of this antibiotic to the usual form of treatment definitely shortened the healing time.

Experiments undertaken by Leopold and Nichols [3] have demonstrated that streptomycin appears in the conjunctiva, sclera, extraocular muscles and aqueous humor of rabbits when it is administered in systemic dosages of 10,000 micrograms per kilogram of body weight. In order that streptomycin might appear in detectable amounts in the cornea, vitreous, chorioretinal tissues and optic nerve, 100,000 micrograms per kilogram of body weight were required. These huge systemic dosages, which were required to obtain a detectable but probably therapeutically inadequate level in these tissues, might under prolonged treatment produce neurotoxic disturbances in man. Fortunately for the ophthalmologist high concentrations of streptomycin in the conjunctival sac may be instantaneously achieved by simple instillation. Furthermore, satisfactory concentrations are readily obtained in the aqueous in the presence of abraded or inflamed corneas and may be obtained even in the presence of an intact cornea if a wetting agent or iontophoresis is employed.[4] Even in the vitreous high concentrations may be safely achieved by the injection of amounts up to 500 micrograms of streptomycin in 0.1 cc. isotonic sodium chloride solution.[4a]

The purpose of this paper is to present results of streptomycin therapy in experimental and clinical ocular infections.

## I. THE EFFECTIVENESS OF STREPTOMYCIN THERAPY IN EXPERIMENTAL OCULAR INFECTIONS WITH CERTAIN ORGANISMS

*A. Treatment of Experimental Corneal Ulcer Due to Bacillus Pyocyaneus.*—Up to recent times the treatment for clinical or experimental ulcer of the cornea due to Bacillus pyocyaneus has been unsatisfactory. Sulfapyridine administered orally to the experimental animal has been ineffective prophylactically, causing only a decrease in the severity of the infection.[5] When sodium sulfacetamide was used locally as a prophylactic agent,[6] the administration of it in one hour prevented 11 of 17 infections; after 5 hours, 5 of 12, and after 12 hours, only 2 of 12. Von Sallmann,[7] employing the same organism and sulfadiazine administered orally and locally by means of iontophoresis, was successful in preventing infection in 90 per cent of the inoculated animals.

Experiments were undertaken to determine the effectiveness of streptomycin in similarly produced corneal ulcers. The strain of B. pyocyaneus used was one which produced uniform infections of the cornea in rabbits. In a series of normal rabbits anesthetized by intravenous injections of pentobarbital sodium, an area of each cornea was delineated by a 4 mm. trephine and the epithelium within this area was abraded by a knife. Fluorescein was employed to determine the completeness of abrasion, after which a cotton applicator moistened in a twenty-four hour broth culture of B. pyocyaneus was forcibly rubbed against the abraded area of both eyes for sixty seconds.

Fig. 1.—Pyocyaneus infection of cornea untreated.

Streptomycin was applied to the right eye at two, four, six, eight and twenty-four hours after inoculation, while the left eye was reserved as an untreated control. Treatment consisted of three instillations of an isotonic sodium chloride solution containing 10,000 micrograms of streptomycin per cubic centimeter at two hour intervals after the periods previously indicated.

Our experiments demonstrated that streptomycin therapy, when applied within six hours, in all cases prevented infection of the cornea. The control eyes uniformly progressed to complete destruction of the cornea. These results indicate the great value of streptomycin against B. pyocyaneus in infections of the cornea. Up to the present time, streptomycin is unexcelled as a therapeutic agent in this type of infection (figs. 1 and 2).

*B. Treatment of Experimental Streptococcic Infection of Vitreous.*—Attempts to prevent or influence experimental infections of the vitreous had been unsuc-

From Northwestern University Medical School.

The work described in this paper was done under a contract between the Navy Program for Basic Research and Northwestern University.

Read before the Section on Ophthalmology at the Ninety-Sixth Annual Session of the American Medical Association, Atlantic City, N. J., June 12, 1947.

1. Owens, W. C.: Streptomycin Treatment of Corneal Infections, Am. J. Ophth. **29**: 1007-1009 (Aug.) 1946.
2. Alberstadt, N. F., and Price, A. H.: Streptomycin for Corneal Ulcer, Am. J. Ophth. **29**: 1106-1111 (Sept.) 1946.
3. Leopold, I. H., and Nichols, A.: Intraocular Penetration of Streptomycin Following Systemic and Local Administration, Arch. Ophth. **35**: 33-38 (Jan.) 1946.
4. (*a*) Bellows, J. G.; Burkholder, M., and Farmer, C. J.: to be published. (*b*) Leopold and Nichols.[3]
5. Joy, H. H.: Treatment of Experimental Bacillus Pyocyaneus Ulcer of Cornea with Sulfapyridine, Arch. Ophth. **27**: 1135-1164 (June) 1942.
6. Robson, J. M., and Scott, G. I.: Local Effectiveness of Sodium Sulphacetamide (Albucid Soluble) in Treatment of Experimental Ulcers of the Cornea, Brit. M. J. **1**: 5-8 (Jan. 3) 1942.
7. von Sallmann, L.: Sulfadiazine Iontophoresis in Pyocyaneus Infection of Rabbit Cornea, Am. J. Ophth. **25**: 1292-1300 (Nov.) 1942.

cessful until von Sallmann and his co-workers [8] and Leopold [9] were able to check the progress of a hemolytic Staphylococcus aureus infection and Klebsiella pneumoniae type III infection by means of the intravitreous injection of penicillin. The present experiment was to determine the effectiveness of streptomycin therapy with experimental beta-hemolytic streptococcic infection of the vitreous. For this purpose the vitreous of each eye of a series of rabbits was inoculated with 0.1 cc. of a twenty-four hour broth culture of Streptococcus pyogenes strain C 203 diluted to 1:10,000 in isotonic sodium chloride solution (plate count 1,000 to 2,000 organisms per cubic centimeter). This organism was observed to be sensitive to 10 micrograms of streptomycin in 1 cc. of solution.

These rabbits were treated either systemically or by injection of streptomycin into the vitreous. The systemic administration was in the form of (1) continuous intravenous drip of 100,000 micrograms of streptomycin solution per kilogram of body weight over a period of six hours or (2) intramuscular injection of a similar amount of the agent emulsified in a sterile preparation of cholesterol derivatives in peanut oil with

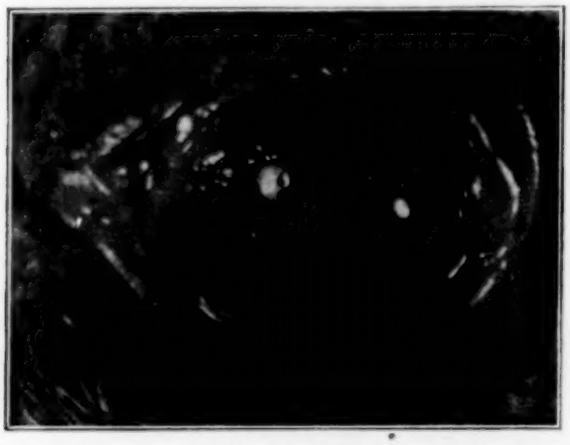


Fig. 2.—Pyocyaneous infection of cornea treated with streptomycin.

2 per cent beeswax ("pendil improved"); the drug was given either as a prophylactic or therapeutic measure. The intravitreal injections of streptomycin were administered either simultaneously or two, four, six, eight or twenty-four hours after the inoculation. For intravitreous injection 0.1 cc. of an isotonic solution of sodium chloride containing 250 to 1,000 micrograms of streptomycin per cubic centimeter was used.

In these experiments neither form of systemically administered streptomycin prevented the development of a vitreous abscess. However, the external inflammatory manifestations were far less pronounced in the systemically treated animals than in untreated controls. Animals receiving intravitreous injections of 100 to 200 micrograms of the less purified streptomycin, or as little as 25 micrograms of the streptomycin–calcium chloride complex did not develop a vitreous abscess if treated within six to eight hours after the inoculation. On the other hand, vitreous infection resulting in eventual abscess occurred in the untreated control eye or in those treated with less than the previously specified amounts of streptomycin (fig. 3).

As noted by Leopold and Nichols, streptomycin enters the vitreous with difficulty. Concentrations of but 2 units of the agent per gram of vitreous could be obtained following a single intramuscular injection of 100,000 units of streptomycin per kilogram of body weight. Since the in vitro sensitivity of the organism employed by us was shown to be 10 micrograms per cubic centimeter, it is easy to understand why the systemic administration of the antibiotic was ineffective. The observed higher concentrations reported by Leopold and Nichols as occurring in the conjunctiva, sclera, extraocular muscles and aqueous humor explains the localization of the infection to the vitreous. On the other hand, the direct intravitreal injection of streptomycin in the concentrations and within the time indicated effectively prevents infection. Our experimental results parallel those of Leopold and of von Sallmann, who demonstrated that vitreous infection with staphylococci or pneumococci were arrested if intravitreal injections of penicillin were made within eight hours after inoculation.

### II. THE CLINICAL APPLICATION OF STREPTOMYCIN IN OCULAR INFECTIONS

In 23 cases of ocular infections treated with streptomycin, 7 were acute conjunctivitis, 10 were chronic conjunctivitis, 5 were corneal infections and 1 was a postoperative intraocular infection.

*A. Acute Conjunctivitis.*—The 7 cases of acute conjunctivitis included 1 primary meningococcic conjunctivitis, the organism being identified as Neisseria intracellularis group IIa. There was 1 patient with almost a pure culture of Bacillus subtilis and another with a pure culture of diphtheroids. Hemolytic staphylococcus albus and alpha hemolytic streptococci were found in 1 case; hemolytic Staph. albus alone in 1 case, and hemolytic Staph. albus with diphtheroids in another. In 1 patient cultures and smears were negative. The general procedure for all patients was to give streptomycin drops (10,000 micrograms per cubic centimeter) at one hour intervals during the waking hours (eight to nine applications a day) and to continue the treatment for eight days.

The meningococcic conjunctivitis improved in twenty-four hours, and the eye appeared normal at the end of four days (figs. 4 and 5). The infection due to B. subtilis showed improvement in forty-eight hours, and the redness was entirely gone by the seventh day. The conjunctiva from which the pure culture of diphtheroids was obtained was greatly improved by the third day and entirely well on the seventh day. In the case in which there was a mixed infection due to hemolytic Staph. albus and alpha hemolytic streptococcus, improvement was evident in forty-eight hours. The patient in whom infection was due to hemolytic Staph. albus alone recovered completely by the seventh day, and the patient with acute conjunctivitis in which no organisms were isolated recovered on the fourth day.

*B. Chronic Conjunctivitis.*—There were 10 cases of chronic conjunctivitis. The duration of the disease prior to streptomycin therapy varied from one month to several years. In 3 of these the smears and cultures were negative, and treatment with streptomycin pro-

8. (*a*) von Sallmann, L.; Meyer, K., and Di Grandi, J.: Experimental Study of Penicillin Treatment of Ectogenous Infection of Vitreous, Arch. Ophth. **32**: 179-189 (Sept.) 1944. (*b*) von Sallmann, L.: Penicillin Therapy of Infections of the Vitreous, ibid. **33**: 455-462 (June) 1945.

9. Leopold, I. H.: Intravitreal Penetration of Penicillin and Penicillin Therapy of Infections of the Vitreous, Arch. Ophth. **33**: 211-216 (March) 1945.

duced no noticeable change in symptoms. In 1 case there was a chalazion associated with a decided conjunctival inflammation of both the upper and the lower lids. Culture from the conjunctiva revealed two colonies of hemolytic Staph. aureus, three colonies of alpha Strep. fecalis and five colonies of diphtheroids. Streptomycin drops, although causing the conjunctival sac to become sterile, produced no appreciable improvement in the appearance of the eye in eight days. In another patient hemolytic staphylococci and diphtheroids were found. After forty-eight hours of therapy a culture from the conjunctiva was negative. There was pronounced improvement both objectively and subjectively. Treatment was continued for eight days. However, three weeks after the cessation of treatment there was a recurrence of symptoms. In 1 case pneumococci were found. After six days of streptomycin therapy cultures from the conjunctivas became negative. However, the conjunctivas remained red and the discomfort continued even after ten days of therapy, after which treatment was discontinued. In a chronic case of fifteen years' duration, a culture of material from the right eye exhibited the growth of one colony of coagulase-negative Staph. aureus, while that from the left produced eight colonies. After three days of streptomycin therapy cultures exhibited no growth and subjective symptoms were improved.

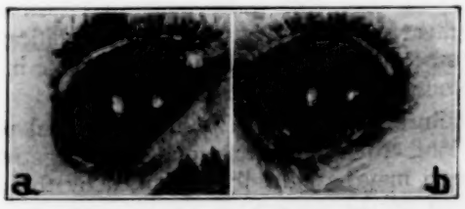



Fig. 3.—Vitreous infection (*a*) untreated and (*b*) treated.

However, the palpebral conjunctivas were still hyperemic even after ten days of treatment. A smear taken from another patient revealed a single gram negative extracellular organism, but the cultures were negative. Streptomycin therapy was stopped after forty-eight hours because the patient stated that the treatment "made the eye feel and look worse."

The final test of the clinical application of streptomycin was in a patient with myotonic dystrophy with typical cataracts. He had suffered from chronic conjunctivitis for many years. There were scars in the palpebral conjunctivas of the two upper lids and in the vessels in the corneas. Conjunctival scrapings which were dyed with Giemsa's stain failed to reveal any inclusion bodies. Cultures were negative. Local streptomycin therapy caused a decided decrease in the conjunctival congestion and secretion within seven days.

*C. Corneal Infections.*—There were 5 cases of corneal disease. One patient had corneal infection which, despite treatment for three months with fever therapy, sulfonamide drugs, penicillin and delimiting keratotomy, continued to progress. Before local streptomycin therapy was instituted smears and cultures were taken from the ulcer. These failed to exhibit the growth of any organisms. Within five days the cornea no longer stained with fluorescein, the margins of the lesions became more distinct and there was a pronounced decrease in the generalized congestion.

The second case was that of a white man aged 40, who was in a poor state of general nutrition. There was a slowly progressive corneal infiltration of the left eye accompanied by exudates in the anterior chamber. His previous treatment had consisted in attempts to improve the general nutrition and local treatment

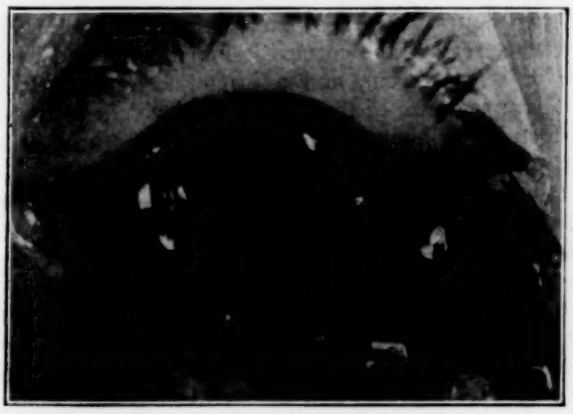


Fig. 4.—Meningococcic conjunctivitis before treatment.

in the form of atropine, sulfonamide compounds, penicillin by drops and iontophoresis and delimiting keratotomy. Cultures taken prior to streptomycin therapy revealed ten colonies of diphtheroids and forty colonies of a gram-negative rod. Local streptomycin therapy for ten days did not change the course of the disease.

The third corneal infection was a long standing, active, tuberculous keratitis having characteristics of both phlyctenular and interstitial types. Atropine therapy and tuberculin desensitization had been without effect. Streptomycin was administered in the form of drops and iontophoresis without apparent improvement in ten days, at which time treatment was discontinued.

In the fourth case a Negro man had a deep grayish white infiltrate in the cornea. Four days of fever

Fig. 5.—Meningococcic conjunctivitis after four days of streptomycin therapy.

therapy and local instillations of atropine failed to stop the progress of the disease. A culture taken from the cornea at this time revealed twenty colonies of hemolytic Staph. albus and one hundred and thirty colonies of diphtheroids. Streptomycin in the form of drops was administered at two hour intervals. A definite improvement was noticed in forty-eight hours.

The fifth patient was admitted to the hospital on the service of Dr. I. Puntenney. There was a severe rapidly progressive pyocyaneus infection of the cornea, which had been unresponsive to sulfonamide drugs. At the beginning of the third day of the infection 2 or 3 drops of the solution of streptomycin were instilled into the infected eye every thirty minutes during the waking hours and every two hours at night. Any further spread of the corneal lesion was blocked by the use of streptomycin, and a pronounced improvement in the appearance of the eyeball was evident at the end of forty-eight hours. The redness disappeared at the end of the seventh day.

*D. Intraocular Infection.*—A Japanese patient on Dr. B. Cushman's service was seen on the second postoperative day after an intracapsular extraction. Examination revealed a well defined conjunctival congestion, but the cornea was fairly clear. In the pupillary area a yellowish gray exudate was present. Cultures revealed a hemolytic Staph. aureus. It was recommended that penicillin and streptomycin be administered by means of iontophoresis. On the fourth day 1,000 Oxford units of penicillin and 500 micrograms of streptomycin were injected into the anterior chamber. The course of the infection was not influenced by these antibiotics.

## COMMENT

In the evaluation of streptomycin therapy the rapidity of improvement must be considered in both acute and chronic ocular infections. In acute infections if the period of morbidity under streptomycin therapy is constantly less than that observed in treatment by earlier conventional methods, it may be assumed that the drug was responsible for this favorable effect. In chronic infections which have resisted other forms of therapy, if rapid improvement follows the use of streptomycin it is at least suggestive that the improvement is attributable to this agent. Ideally, observations on the therapeutic effectiveness of a new agent should be based on cases of bilateral infection which permit adequate controls, the more severely infected eye receiving the therapeutic agent while the other receives an equal amount of the vehicle. This was attempted in 2 of the cases reported herein without significant results.

The use of streptomycin instead of penicillin in certain infections due to organisms known to be sensitive to penicillin is justified on the basis of Robinson's [10] observations and of our determination of the sensitivity of the organisms. Furthermore, it would be valuable to be able to use another drug in the treatment of those persons who are hypersensitive to penicillin in cases in which the organism has acquired a resistance to penicillin, or in combination with penicillin in some instances of mixed infections.

As anticipated from Robinson's in vitro experiments, which demonstrated the high degree of sensitivity of the meningococcus to streptomycin, the acute meningococcic conjunctivitis responded rapidly to treatment with this antibiotic. The improvement noted in the other 6 cases of acute conjunctivitis produced by a variety of organisms indicates that streptomycin may be useful in the treatment of some forms of this disease. However, the value of this antibiotic cannot be definitely established until many more instances have been observed, particularly in cases of bilateral infection with adequate controls established by the procedure previously suggested.

In all 6 cases of chronic conjunctivitis in which organisms were found in the conjunctivas just prior to streptomycin therapy, the cultures became sterile a few days later. However, the clinical appearance in some instances was unchanged, suggesting that other than bacterial causes were active in continuing the inflammation. Streptomycin exerted a favorable influence in the case of chronic conjunctivitis with the clinical characteristics of trachoma.

In our animal experiments streptomycin was found to be completely effective in the prevention of corneal infections due to B. pyocyaneus if used within six hours. Its value in this disease has been further established by our clinical observations in the case of B. pyocyaneus infection of the cornea of forty-eight hours' duration which responded promptly to streptomycin. The favorable influence of streptomycin in the rapidly advancing infection of the cornea (fourth case) from which hemolytic Staph. albus and diphtheroids were cultured is also noteworthy. In the slowly advancing corneal ulcer which had progressed in spite of all other forms of treatment it is significant that improvement occurred concomitantly with the initiation of streptomycin therapy.

The failure of streptomycin in the corneal ulcer in which diphtheroids and numerous gram-negative rods were found may be partially explained by the general debilitation of the patient.

Finally, the keratitis which had characteristics of both the phlyctenular and interstitial types also failed to improve, even with intensive streptomycin therapy. If the condition was entirely phlyctenular in nature no improvement could be expected, since this type of keratitis is due to a hypersensitization to tuberculin protein.

Von Sallmann in both clinical and animal studies reported the refractory nature of advanced infections of the vitreous to penicillin. This is also true with streptomycin, for as shown in the early part of this paper no arrest of the infection occurred in rabbits if streptomycin therapy was instituted eight hours after inoculation with the infective organism. This explains the failure of the well established postoperative intraocular infection to respond to antibiotics. However, if postoperative intraocular infections can be recognized within the specified time limits in which the antibiotic is effective, the injection of the agent directly into the eye might arrest the infection and thus save the eye.

From our clinical observations it is evident that many organisms are soon eliminated from the conjunctiva and cornea by repeated instillations of streptomycin solution in the recommended concentrations. In many instances recovery from certain types of acute and chronic external ocular infections will follow the disappearance of the organisms. Relapses occur if treatment is stopped too soon. Inflammatory conditions in which organisms are not isolated cannot be expected to respond to streptomycin therapy, nor do infectious dis-

10. Robinson, H. J.: Streptomycin and Streptothricin: The Absorption, Excretion, and Chemotherapeutic Properties: Antibiotics, Ann. New York Acad. Sc. **48**: 119-141 (Sept.) 1946.

eases in which other contributing factors are present, such as chalazion or general debilitating diseases, respond to streptomycin therapy alone.

SUMMARY

The penetrability of the cornea to streptomycin may be increased by abrasion, inflammation, ion transfer and wetting agents.

Streptomycin is safe and nonirritating to the surface of the eyeball in concentrations up to 10,000 micrograms per cubic centimeter. Higher concentrations delay the regeneration of the epithelium and promote scarring and vascularization of the cornea.

Intraocular injections of 500 micrograms of streptomycin in 0.1 cc. of isotonic sodium chloride solution are well tolerated. However, as little as 25 micrograms of streptomycin is effective in the prevention of experimental beta hemolytic streptococcic infections of the vitreous if the drug is injected within six to eight hours after inoculation.

Experimental corneal infections due to Bacillus pyocyaneus are completely prevented if within six to eight hours after inoculation three instillations of streptomycin drops (10,000 micrograms per cubic centimeter) are made at two hour intervals.

Repeated instillations of 10,000 micrograms of streptomycin in 1 cc. of isotonic sodium chloride solution sterilizes the conjunctival sac in most cases of acute and chronic conjunctivitis.

Clinically streptomycin was employed in 23 cases of ocular infection. In 2 cases it was exceptionally effective, namely, a primary meningococcic conjunctivitis and a B. pyocyaneus infection of the cornea.

There is definite evidence that in most cases both of acute and of chronic infections of the conjunctiva and cornea organisms are rapidly eliminated by streptomycin therapy; in the absence of complicating factors healing follows rapidly in many instances.

## ABSTRACT OF DISCUSSION

DR. PARKER HEATH, Detroit: The evaluation of the merits of a new antibiotic in the field of ocular therapy is no easy task. There are certain requisites, such as controlled laboratory testing and extended and versatile clinical investigation. Both of these approaches should be made by open, truth-seeking minds. Dr. Bellows and Dr. Farmer are reporting along these avenues. Their laboratory studies support those of Leopold and Nichols, that effective concentrations of streptomycin in ocular tissue could not be had by practical, systemic application and that local use was effective in the antibiotic range of the drug, local use by topical application and supported by wetting agents, corneal scuffing or iontophoresis as advocated by von Sallmann (10,000 micrograms per cubic centimeter at two hour intervals). In the vitreous, the most effective minimal concentration followed direct injection of 100 to 200 micrograms of the sodium and 2.5 micrograms of the calcium chloride complex. All this is consistent with other reported studies by Leopold and von Sallmann on the use of sulfonamide compounds or penicillin. While the clinical series of the authors is too small to be conclusive, good clinical hints are extractable. Streptomycin seems unusually effective in meningococcic conjunctivitis and keratitis due to Pseudomonas aeruginosa—the latter being based on animal experimentation and 1 human case. Hemolytic Staphylococcus albus and alpha hemolytic Streptococcus were in the range of the drug. Owens and Alberstadt and Price have reported success from local use. The failure of response in active ocular tuberculosis in 1 case is consistent with the experiences of others. The first ray of hope in a chemotherapeutic attack on ocular tuberculosis is that recently reported by Woods, using "promin" (sodium p,p'-diaminodiphenylsulfone-N,N'didextrose sulfonate) and "promizole" (4,2'-diaminophenyl-5'-thiazolylsulfone) in experimental ocular tuberculosis in immune allergic rabbits. Bellows and Farmer have reported a single case of postoperative infection which failed to yield to both iontophoresis and streptomycin on the second day and injections into the anterior chamber on the fourth day. This is not conclusive, because of the lateness of the treatment. Ophthalmic surgery has a low incidence of postoperative infection. But the complication is a probability which no one can completely deny. The authors have shown early effective concentration to be necessary. This is in support of my practice of inspecting eyes after intraocular surgical treatment within twenty-four hours. In my experience, the complications from systemic use of streptomycin are real—those from local use are not so significant. Locally there is delayed epithelization of the cornea and some promotion of scar. A confusing probability is that of adaptability of the infectious organism to streptomycin.

DR. IRVING H. LEOPOLD, Chicago: For many years Dr. Bellows and his associates have contributed substantially to our knowledge of the new chemotherapeutic agents. He has studied both experimentally and clinically numerous sulfonamide compounds, penicillin and now streptomycin. He is therefore in an excellent position to evaluate carefully any new anti-infectious agent. The evidence accumulated by Dr. Bellows and Dr. Farmer seems to favor the local methods of applying streptomycin over systemic administration for many types of ocular infections. Conjunctivitis, keratitis and infections of the vitreous are examples. There are many reasons for this. Systematically administered streptomycin is not free of toxic properties. Monkeys receiving injections of 50 to 100 mg. per kilogram of body weight showed a peculiar type of fatty infiltration of the kidneys and of the liver. The same dose caused proteinuria and some reduction of renal function. Dogs given similar doses occasionally had labyrinthine disturbances, a phenomenon that has also been noted in human beings and probably represents streptomycin's most serious untoward effect. Local tissue toxicity, however, is not pronounced. It is true that application of 1,250 units of streptomycin to the cerebral cortex of cats and monkeys has caused convulsive manifestations in 30 per cent of the animals tested, but these effects were less strong than those produced by comparable amounts of penicillin—as judged by clinical and encephalographic observations. Streptomycin has a low toxicity for spleen in tissue culture and is only mildly inhibitory for fibroplasts and epithelial cells. One of the chief disadvantages of streptomycin is the ease with which organisms develop a resistance to this drug. This is less likely to occur if the concentrations of the streptomycin in the infected tissues are high and maintained. It has been shown that higher concentrations can be obtained in most of the ocular tissues by local administration than by the systemic route. This is certainly the case for the conjunctiva, cornea, anterior chamber, vitreous humor and lens. To recommend local therapy for inflammations of ocular tissues does not mean that the systemic route may not also be successful in some types of ocular infections but simply that systemic therapy is not necessary for ocular infections not associated with systemic disease, may be more dangerous and, in addition, is more expensive, as tremendously greater quantities are required.

DR. JOHN G. BELLOWS, Chicago: I wish to thank Dr. Heath for his interesting remarks. He and Dr. Leopold mentioned that the organisms develop resistance to streptomycin readily. An organism that is at first sensitive to streptomycin may become within twenty-four hours resistant to it. Dr. Leopold has called our attention to the dangers inherent in the systemic use of streptomycin. Hypersensitization is relatively uncommon with the external application of streptomycin. This is indicated by the development of sensitization in only 1 of 30 cases in which this antibiotic was used.

# THE CONTROL OF EPILEPSY

## An Interim Report on 3-Methyl-5, 5-Phenylethylhydantoin and Phenobarbital Therapy

ANTHONY E. LOSCALZO, M.D.
New York

A preliminary report by me in 1945 [1] dealt with a two year study of a new anticonvulsant, 3-methyl-5, 5-phenylethylhydantoin [2] and phenobarbital in a group of patients suffering from epilepsy of unknown or organic etiology. This new drug reduced grand mal seizures approximately 60 per cent, as compared to previous medications with diphenylhydantoin sodium and phenobarbital. It is important to note that phenobarbital was used in combination with both diphenylhydantoin sodium and 3-methyl-5, 5-phenylethylhydantoin, thus assuring a valid comparison of the two drugs. The incidence of side effects with the latter as compared with diphenylhydantoin sodium was strikingly low.

It was suggested in the first report that further investigations were indicated and necessary for more complete evaluation. This interim report is a continuation of the preliminary studies and encompasses an additional eighteen months of observation on the same patients and 51 new patients.

Since the first publication additional experimental data has accumulated. Swinyard and Goodman,[3] studying a group of hydantoinates in rats, introduced two new laboratory technics:

> The toxic dose (*T*) was taken as that just causing observable neurological deficit or other untoward effect. The protective dose (*P*) was that just required to abolish tonic extensor components of maximal electroshock seizures produced by current intensities five times threshold.

In this report by Swinyard and Goodman [3] it was noted that the protective index (*T*/*P*), which is the ratio of the toxic dose to the protective dose, has a value of 12 for 3-methyl-5, 5-phenylethylhydantoin and 2 for diphenylhydantoin sodium. In the same report it was stated that the percentage change in normal electroshock threshold was plus 27 for 3-methyl-5, 5-phenylethylhydantoin and only plus 2 for diphenylhydantoin sodium.

These authors also observed that the dose (milligram per kilogram intraperitoneally) for protection against maximal electroshock seizures was 5 mg. with 3-methyl-5, 5-phenylethylhydantoin and 50 mg. for diphenylhydantoin sodium.

These data suggest in animals pronounced advantages for 3-methyl-5, 5-phenylethylhydantoin and thus aid in substantiating the clinical observations in these studies up to this time.

### CHEMICAL NOTES ON 3-METHYL-5, 5-PHENYLETHYLHYDANTOIN

The structural formulas (figs. 1, 2 and 3) show the close chemical similarity and relationship between some of the most commonly used anticonvulsants, including 3-methyl-5, 5-phenylethylhydantoin, on which this clinical study is based.

Diphenylhydantoin sodium and 3-methyl-5, 5-phenylethylhydantoin are both hydantoin derivatives. They may be considered as derivatives of a cyclic condensation product of urea and acetic acid, whereas phenobarbital is a derivative of the cyclic condensation product of urea and malonic acid.

As to the chemical difference between diphenylhydantoin sodium and 3-methyl-5,5-phenylethylhydantoin, it is noted that one phenyl group of the diphenylhydantoin sodium is replaced by an ethyl group in 3-methyl-5, 5-phenylethylhydantoin; in addition, one hydrogen atom, bound to nitrogen, is replaced by a methyl group in the new drug. Furthermore, diphenylhydantoin sodium is offered in the form of the sodium compound, whereas 3-methyl-5, 5-phenylethylhydantoin is sodium-free and has the chemical characteristics of a weak acid.

### CLINICAL STUDIES

Of the 67 cooperative patients studied,[4] 35 were females and 32 males; 16 patients were of the original group reported in the preliminary studies of 1945. Electroencephalograms were performed on 54 patients; pneumoencephalograms on 12, roentgen examination of the skull on 28, and exploratory craniotomy on 5. The Wassermann test, complete blood count, urinalysis and blood chemical studies (dextrose, urea nitrogen and creatinine) were done routinely on all patients. Blood calcium, phosphorus studies, dextrose tolerance tests and basal metabolism determinations were ordered when indicated. All patients were subjected to a complete neuropsychiatric check-up. The history and physical examination forms of the American Epilepsy League are standard in this clinic.

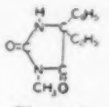


Figure 1.

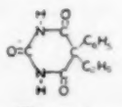


Figure 2.

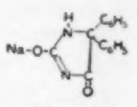


Figure 3.

Fig. 1.—"Mesantoin," 3-methyl-5,5-phenylethylhydantoin.
Fig. 2.—"Dilantin sodium," Diphenylhydantoin sodium.
Fig. 3.—Phenobarbital, phenylethylbarbituric acid.

Each patient was seen at the clinic once each week for the first few weeks and then every second week or monthly, depending on the severity and frequency of the attacks. Each patient was instructed to bring in a written record of the date, time and severity of each convulsion as well as a description of any untoward symptoms that were experienced. At each visit these facts were transcribed and further histories taken and physical examinations made when indicated. When patients failed to attend a clinic a postal card was mailed asking them to return. Data on the noncooperative patients are excluded from this study.

The age range of the sixty-seven patients is given in table 1, and the duration of epilepsy in table 2. The duration of treatment with 3-methyl-5, 5-phenylethylhydantoin is shown in table 3. According to the Lennox Classification,[5] the cases fall into one of the groups shown in table 4.

The figures represent the predominant type of seizure in each patient, but all patients, except one traumatic jacksonian, suffered from grand mal and many of the patients, in addition, had petit mal.

1. Loscalzo, A. E.: Treatment of Epileptic Patients with a Combination of 3-Methyl 5, 5 Phenylethyl-Hydantoin and Phenobarbital (Preliminary Report), J. Nerv. & Ment. Dis. **101**: 537 (June) 1945.

2. This drug is available as "mesantoin," a product supplied by Sandoz Chemical Works, Inc.

3. Swinyard, E. A., and Goodman, L. S.: Laboratory Assay of Anticonvulsant Potency of Some Hydantoinates, Federation Proc. **5**: 205 (Feb.) 1946.

4. From the Clinic for Convulsive Disorders, Columbus Hospital; Dr. David J. Impastato, Director.

5. Lennox, W. G.: The Treatment of Epilepsy, M. Clin. North America **29**: 1114 (Sept.) 1945.

The probable etiologic basis for the disease is given in table 5. In the group of 51 cases of undetermined cause are included 5 cases with positive neurologic observations suggestive of chronic degenerative disease, 1 case of chronic alcoholism, 1 case of neurosyphilis (latent) and 1 case of mild manic-depression. This also holds true for some cases in which the electroencephalograms showed possible epileptogenous areas. It might be argued that the etiologic basis was evident in some of these cases, but there were so many controversial points that it was decided to place them in the group of undetermined cause. The 3 cases of cortical degeneration were proved by surgical operation.

### PREVIOUS MEDICATION

Fifty-five patients had been taking diphenylhydantoin sodium in varying amounts; most of them were taking 3 capsules, 0.3 Gm. (4.5 grains) to 5 capsules, 0.5 Gm. (7.5 grains) per day, the highest being 0.6 Gm. (9 grains) per day. Fifty of the 55 had been taking the diphenylhydantoin sodium in combination with phenobarbital; 8 of them had been receiving 0.03 to 0.06 Gm. (½ to 1 grain) of phenobarbital daily; 11, over 0.06 Gm. (1 grain) to 0.1 Gm. (1½ grains) daily; 23, over 0.1 Gm. (1½ grains) to 0.13 Gm. (2 grains) daily; 8, over 0.13 Gm. (2 grains).

Only 5 patients had taken diphenylhydantoin sodium alone. Ten had been unable to take this drug due to toxic effects. Two had never taken diphenylhydantoin sodium but had received phenobarbital alone. All the patients had taken phenobarbital alone or in conjunction with bromides or other barbiturates prior to diphenylhydantoin sodium therapy.

TABLE 1.—*The Age Range of Sixty-Seven Patients with Epilepsy*

| Years | Number of Patients | |
|---|---|---|
| 6 to 10 | 9 | |
| 11 to 20 | 13 | 44 patients |
| 21 to 30 | 20 | (ages 11 to 40) |
| 31 to 40 | 11 | 65% of total |
| 41 to 50 | 6 | |
| 51 to 60 | 6 | |
| 61 to 70 | 2 | |

Approximately 50 per cent of the patients reported that diphenylhydantoin sodium had reduced the frequency and severity of their grand mal attacks. The other half did not report any significant results. Of all the patients (42 cases) taking up to 0.13 Gm. (2 grains) of phenobarbital with the diphenylhydantoin sodium daily, none reported sufficient drowsiness to cause any interference with daily activities, although the degree of drowsiness varied in individual cases. Many of them agreed that "slight drowsiness was more noticeable in the beginning when I started to take the little white pills, but I do not feel it now. I guess I am used to it." An appreciable tolerance to phenobarbital in almost all patients is apparently established early.

Depending on the severity and frequency of the attacks, 1 to 6 tablets of 3-methyl-5, 5-phenylethylhydantoin and 0.02 to 0.13 Gm. (⅓ to 2 grains) of phenobarbital were taken by each patient daily; the average dose being 4 tablets, 0.4 Gm. (6 grains) of 3-methyl-5,5phenylethylhydantoin and 0.088 Gm. (1⅓ grains) of phenobarbital daily. Kozol's[6] average dose in his initial studies was 0.6 Gm., or 6 tablets, of 3-methyl-5, 5-phenylethylhydantoin daily, but with longer experience he at present considers that the average adult dose is higher. The favorable action of phenobarbital is suggested when it is noted that, in this series, comparative therapeutic results are obtained with an average dose of 4 tablets (0.4 Gm.) of 3-methyl-5,5-phenylethylhydantoin and 0.088 Gm. (1⅓ grains) of phenobarbital daily.

6. Kozol, H. L.: Epilepsy: Treatment with New Drug, 3-Methyl 5, 5-Phenyl-Ethyl-Hydantoin (Phenantoin), Am. J. Psychiat. **103**: 154 (Sept.) 1946.

TABLE 2.—*Duration of Epilepsy*

| Years | Number of Patients | |
|---|---|---|
| 0 to 5 | 19 | 54 patients |
| 6 to 10 | 20 | 80% of total aged |
| 11 to 15 | 15 | 15 years or less |
| 16 to 20 | 5 | |
| Over 20 | 8 | |

The average duration was approximately eleven years

TABLE 3.—*Duration of Treatment with 3-Methyl-5, 5-Phenylethylhydantoin*

| Months | Number of Patients | | |
|---|---|---|---|
| 0 to 5 | 7 | | |
| 6 to 10 | 12 | 50% of total patients took | |
| 11 to 15 | 9 | the drug 2 years or less | |
| 16 to 20 | 5 | | |
| 21 to 25 | 4 | | 50% of total |
| 26 to 30 | 8 | | patients took |
| 31 to 35 | 10 | 33% of total patients took | the drug over |
| 36 to 40 | 12 | the drug almost 3 years | 2 years |

### CLINICAL RESULTS

This study is now in its fourth year, which is a reasonable length of time to fairly evaluate therapeutic results. The average expected incidence figure is derived from the number of grand mal attacks each patient experienced during the previous twelve months on the former therapy prior to beginning the new drug. It is to be assumed that this number of major seizures would continue if the new drug had not been given. Of course, it is important to note that many patients experience spontaneous remissions of varying periods, which always complicate any study of therapeutic results in epilepsy. In the majority of cases improvement followed almost immediately, so that the question of spontaneous remissions can hardly play an important role. In addition many of the patients who no longer had any seizures after a reasonable period of

TABLE 4.—*Classification of the Types of Seizures*

| Types of Seizures | Number of Patients |
|---|---|
| Grand mal | 45 |
| Psychomotor | 12 |
| Petit mal | 5 |
| Focal convulsions | 3 |
| Myoclonic | 1 |
| Jacksonian | 1 |

TABLE 5.—*Probable Etiology*

| Types | Number of Patients |
|---|---|
| Undetermined | 51 |
| Trauma | 6 |
| Birth injury | 4 |
| Arteriosclerosis | 3 |
| Cortical degeneration | 3 |

time while taking 3-methyl-5, 5-phenylethylhydantoin had the dosage reduced, and in almost all cases a reappearance of grand mal seizures was again reported. Two of these patients had not had any seizures in three years.

The total average expected incidence of grand mal seizures in the 67 patients was 2,891. The actual number of grand mal attacks experienced by these same patients taking 3-methyl-5, 5-phenylethylhydantoin and phenobarbital was 1,140. This represents a reduction in the number of major seizures of approximately 60 per cent. In some cases petit mal and psychomotor seizures were also reduced, but these data were insufficient to be of any statistical value. However, Kozol [7] states that "this drug appears to be highly effective against psychomotor attacks."

In the single case of jacksonian epilepsy of traumatic origin this new anticonvulsant gave dramatic results. The patient, a man aged 45, had been having right lower extremity seizures for seven years. Three outstanding neurosurgeons after thorough and careful examinations agreed that operative measures would be of no avail. The man was taking 8 capsules of diphenylhydantoin sodium, 0.8 Gm. (12 grains) daily and 0.13 Gm. (2 grains) of phenobarbital in divided doses of 0.03 Gm. (½ grain) four times a day. He tolerated this dosage well, and the jacksonian seizures had been reduced from about ten to fifteen daily to about three to five daily. He had voluntarily attempted to increase the dosage of diphenylhydantoin sodium, but it made him nauseated so he continued on 8 capsules daily. Since the seizure of this patient was classified as severe, he was asked to take 0.8 Gm., or 12 grains (8 tablets), of 3-methyl-5, 5-phenylethylhydantoin and 0.17 Gm., or 2⅔ grains, of phenobarbital daily. The seizures ceased promptly. He has had three light jacksonian attacks in one and one-half years since the new regimen was first instituted. In the last three months he has reduced his dosage of the anticonvulsant to only 6 tablets daily without any increase in convulsive movements. This patient's total number of jacksonian seizures has not been included in the expected incidence figure.

Many cases of the predominant grand mal type have resulted in similar dramatic results. In 22 cases, or about one third of the total, the grand mal seizures ceased completely shortly after a regimen of 3-methyl-5, 5-phenylethylhydantoin and phenobarbital was instituted. All these patients, except 1, were in the younger group of 35 years of age or under. The duration of the epilepsy, which varied from one and a half years to twenty years, appeared to play no part in the results of this group. In 7 cases the seizures continued in the same ratio as before the new drug was prescribed. In 6 cases the number of grand mal seizures increased, in spite of adequate dosage and a reasonable trial period. The increase averaged about 10 per cent above the previous incidence. Administration of the drug was discontinued in the latter 6 patients, who were resistant to other types of therapy. In the remaining 32 cases the frequency of grand mal seizures was reduced from 10 per cent to 90 per cent. Of further importance was the fact that the severity of the seizures was definitely lessened. Moreover, most patients experienced fewer postconvulsive ill effects from mild spells than had ensued after the previous severe attacks.

### SIDE EFFECTS

Studies of chronic toxicity in animals have shown the drug to be well tolerated (Spiegel [8]). In this study in 4 cases (6 per cent) there developed gingival hypertrophy; in 3 cases (4.5 per cent) skin rash and in 10 cases (15 per cent) slight drowsiness. Hypertrophy of the gums was minimal in all cases, and the drug was continued. In some cases previous gingival hypertrophy caused by diphenylhydantoin sodium actually receded and disappeared with 3-methyl-5, 5-phenylethylhydantoin therapy. This was especially true in the younger group.

In the 3 cases of skin rash, the rash was generalized and of a morbilliform type. In all cases the rash developed within two weeks. The color varied from pink to deep scarlet, was most pronounced on the extremities, especially the flexor surfaces, and was intensely pruritic. In one case, there was desquamation on the fourth day of the rash. Two of the 3 patients had experienced generalized rash previously, but the cause and description could not be obtained, except that the previous rash had also been pruritic. This suggests that the drug should be given with caution to patients who have had previous generalized rash. Phenobarbital and diphenylhydantoin sodium were ruled out as the possible offenders, since all 3 patients had been taking both drugs for long periods without developing any cutaneous rash. Undoubtedly the new anticonvulsant was the causative factor. The dose in each case was within the average normal of 0.3 to 0.4 Gm. (4.5 grains to 6 grains) daily. Kozol [6] has reported a rash incidence of 10 per cent. This occurred in those patients who were given large initial doses. Recently, however, Kozol [7] has reported that treatment has resulted in virtually no rashes, because he starts with small doses and increases the amount of the drug gradually. Evidently the initial amount of drug taken by dermal sensitive patients determines, in direct proportion, the appearance of the rash with all its clinical manifestations. Some patients require a higher dosage to bring latent sensitivity into activity. In all instances the dosage of the drug was promptly discontinued as soon as the patient reported the cutaneous eruption, and in all 3 patients the rash completely disappeared in approximately ten days. In 1 patient there developed, at the onset of the eruption, an elevation of temperature to 103 F., which was maintained for two days. The other 2 patients reported feeling warm. It is obvious that some elevation in temperature accompanies the rash. Blood counts done at the onset and again at the height of the eruption did not reveal any abnormalities except a moderate leukocytosis. Urinalyses were normal. When the rash had completely disappeared, treatment with the drug was reinstituted and the dosage was slowly increased to the previous therapeutic level. Two of the 3 patients were able to take it again without further toxic effects. The drug was again immediately discontinued in the third patient when pruritus was reexperienced.

Ten patients (15 per cent) complained of drowsiness. In 7 of the 10 cases this side effect was mild.

7. Kozol, H. L.: Personal communication to the author, Oct. 15, 1946.

8. Spiegel, E.: Unpublished data.

None of these patients was taking more than 4 tablets (0.4 Gm., 6 grains) of 3-methyl-5,5-phenylethylhydantoin and 0.088 Gm., or 1⅓ grains, of phenobarbital daily, and all had taken at least 0.06 Gm. (1 grain) of phenobarbital with the diphenylhydantoin sodium previously without complaining of drowsiness. Kozol [6] stated that "the principal drawback or side effect of 'mesantoin' is that it tends to produce drowsiness." This may be due to the fact that Kozol's [6] average dose of 3-methyl-5,5-phenylethylhydantoin for youths and adults was 0.6 Gm. daily (6 tablets), "with individual variations in the adult dosage ranging from 0.3 Gm. daily to over 1 Gm. daily"; while in this clinic, the average dose for adults is 0.4 Gm. daily (4 tablets), which may explain the low incidence of drowsiness. In all cases the drowsiness was most pronounced in the late morning or early afternoon hours. A few patients requiring larger doses in order to maintain a better anticonvulsant effect did complain of a deeper drowsiness. Some of these patients, in whom it was believed that this undesirable effect was due to phenobarbital, were given the 3-methyl-5,5-phenylethylhydantoin with less phenobarbital, but as the dose of the drug approached the daily level of 0.6 Gm., drowsiness increased. It can be deduced, therefore, that the new anticonvulsant has a soporific effect which is in direct proportion to the size of the dose. Children appear to be more sensitive to this effect than adults. After a period of about four weeks this effect lessens, possibly because of an increased tolerance.

None of the patients complained of any gastric disturbances, such as nausea or vomiting. Few patients complained of nervousness, which is a common manifestation of the epileptic state. This may be due to the fact that almost all the patients were also given small doses of phenobarbital. Ataxia and diplopia, which have been reported after treatment with diphenylhydantoin sodium, were not encountered in this series. Ten patients who were unable to take diphenylhydantoin sodium because of toxic symptoms took 3-methyl-5,5-phenylethylhydantoin and phenobarbital without any toxicity whatsoever, and the results in these patients were as good as in the entire series. The toxicity of the new drug is extremely low, as demonstrated by the excessive amounts (72 tablets) taken at one time in a nonfatal suicidal attempt (Kozol [6]). No effect was noted in the blood picture of most of the patients. In about 40 per cent of the cases the lymphocytes were moderately increased at the expense of the neutrophilic polymorphonuclear cells. This observation is being studied further. Routine urinalyses remained unchanged. Blood pressure readings remained the same as before the drug was instituted. No disturbance of the menses was encountered which might be attributed to this drug.

### COMPLICATING ILLNESSES

It would be expected that other illnesses not related to epilepsy would occur in such a group. In 1 patient there developed infectious jaundice, but the jaundice and the other clinical symptoms of this disease cleared up in about three weeks while the patient was on full therapy of 0.4 Gm. (6 grains) of 3-methyl-5,5-phenylethylhydantoin and 0.088 Gm. (1⅓ grains) of phenobarbital daily. In another patient lobar pneumonia developed; 3-methyl-5,5-phenylethylhydantoin (0.3 Gm. daily) and phenobarbital was continued in addition to full doses of sulfadiazine. There were no toxic symptoms, and the pneumonia resolved on the sulfadiazine therapy. One patient suffered a severe skin burn and another fractured an arm in an accident. In both cases satisfactory and normal healing occurred while on full therapy. Four patients became pregnant, and throughout pregnancy full anticonvulsant dosage was continued. No untoward or toxic symptoms were experienced during pregnancy, and all 4 patients underwent normal labors and delivered normal infants.

### ROLE OF PHENOBARBITAL

All physicians interested in the therapy of epilepsy are seeking to find a drug which can be given alone and which will be of benefit in a majority of cases. Up to the present this drug has not been found, and a doubt exists if one drug can satisfy all the varied demands of an epileptic attack, which is in reality a symptom complex. The fact remains that the majority of patients on any type of hydantoin therapy require other drugs, usually of the barbiturate group. Many clinicians prescribe barbiturates in addition to the hydantoin because clinical results are in favor of them. The following investigators, in comparative hydantoin studies, have reported better anticonvulsant results when the drug was given in combination with barbiturates: Doltolo and Bennett,[9] Harris and Ewalt,[10] Weaver, Harrell and Arnold,[11] Robinson and Osgood,[12] Cohen, Showstack and Myerson,[13] Merritt and Brenner [14] and Merritt.[15] Beckman [16] in his 1946 edition of "Treatment in General Practice" states: "As a matter of fact most men find that even in the treatment of adults, 'dilantin' (diphenylhydantoin sodium) is best employed in combination with phenobarbital."

Whether the barbiturate effect is synergistic or otherwise can best be determined from the clinical results. As shown by this and other studies, less hydantoin is required by those patients who also combine with it some barbiturate. Less of the drug would, of course, diminish the possibilities of any toxicity that might result from it in hydantoin-sensitive patients. The amount of barbiturate for this effect is usually small. The proper amount must be determined by careful observation in each case. The addition of a small amount of barbiturate usually decreases further the frequency of the grand mal seizures, lessens the severity of the convulsions, allays the anxiety symptoms of the patient and enables the patient to enjoy a more restful sleep. The latter two points greatly help in improving the patient's general well-being, which is just as important as the decrease in the number of seizures.

9. Doltolo, J. J., and Bennett, C. L.: Some Observations on Treatment of Institutional Epileptics with Dilantin, Psychiatric Quart. **14:** 595 (July) 1940.

10. Harris, T. H., and Ewalt, J. R.: Complications Following the Use of Sodium Diphenylhydantoinate Therapy, J. Oklahoma M. A. **35:** 365 (Sept.) 1942.

11. Weaver, O. M.; Harrell, D. L., and Arnold, G. B.: A Report on the Use of Sodium 5,5-Diphenyl Hydantoinate in Fourteen Selected Cases of Epilepsy at the Virginia State Colony for Epileptics and Feebleminded, Virginia M. Monthly **66:** 522 (Sept.) 1939.

12. Robinson, L. J., and Osgood, R.: Comparative Effects of Phenobarbital and Diltantin Sodium in the Treatment of Epilepsy, J. A. M. A. **114:** 1334 (April 6) 1940.

13. Cohen, B.; Showstack, N., and Myerson, A.: The Synergism of Phenobarbital, Diltantin Sodium and Other Drugs in the Treatment of Institutional Epilepsy, J. A. M. A. **114:** 480 (Feb. 10) 1940.

14. Merritt, H. H., and Brenner, C.: Treatment of Patients with Epilepsy with Sodium Diphenyl Hydantoin and Phenobarbital, J. Nerv. & Ment. Dis. **96:** 245 (Sept.) 1942.

15. Merritt, H. H.: Treatment of Epilepsy, Cincinnati J. Med. **27:** 279 (May) 1946.

16. Beckman, H.: Treatment in General Practice, ed. 5, Philadelphia, W. B. Saunders Company, 1946, p. 802.

COMMENT

This study on the effect of 3-methyl-5,5-phenylethylhydantoin on convulsive seizures was begun in June 1943, and the first clinical report of its effect was published in June 1945.[1] Soon thereafter Clein [17] reported the drug to be more effective in epilepsy than any previous medicament and to be almost free of side effects. One year later, in 1946, Kozol [6] reported that "sixty per cent of the patients in the entire series (104 patients) were either greatly or moderately improved on 'mesantoin' therapy." This included grand mal, psychomotor and focal attacks.

This article represents an interim study of 3-methyl-5,5-phenylethylhydantoin, comprising three years of uninterrupted observation by the same clinician. The results of these studies, as well as those of Clein [17] and Kozol [6] demonstrate definitely that this drug is the most effective in reducing the frequency as well as in lessening the severity of epileptic convulsions. It is also the least toxic of all known hydantoins in use at present. This study has shown that a small amount of phenobarbital increases the anticonvulsant action of this drug. This view is also supported by many other clinicians in respect to diphenylhydantoin sodium.

The drug 3-methyl-5,5-phenylethylhydantoin can apparently be used safely during pregnancy without untoward effects. No other drugs, up to the present writing, have been found incompatible with it. Blood chemistry, renal function and blood pressure appear to be unaffected. The effect on the blood, as already discussed, is being studied further. The drug has been given during certain complicating illnesses with good anticonvulsant effect and no toxic symptoms. Further studies should be done in the jacksonian type seizures. Little influence is exerted on other types of epileptic seizures.

CONCLUSION

In a full three years of study with 3-methyl-5,5-phenylethylhydantoin in 67 cooperative patients, the major portion suffering from epilepsy of undetermined cause and a small number from epilepsy of organic origin, grand mal seizures were reduced approximately 60 per cent and improved emotional status was noted consistently. Other types of epileptic seizures, such as petit mal and psychomotor, were not improved with this medicament. Phenobarbital in small doses increased the anticonvulsant action of this drug and in addition controlled the anxiety and other disturbing symptoms from which many epileptic patients suffer. Less drug was required when combined with small amounts of phenobarbital. The toxicity of 3-methyl-5,5-phenylethylhydantoin is extremely low; only 1 patient was unable to take the drug because of a rash. Other toxic symptoms of hydantoins, such as ataxia, nausea, vomiting, dizziness and diplopia, were not encountered in this series.

This interim study as well as the studies of Clein [17] and Kozol [6] support the preliminary observations of 1945 [1] that 3-methyl-5,5-phenylethylhydantoin is superior to other hydantoins in present use in the treatment of grand mal seizures.

124 East Fortieth Street.

17. Clein, N. W.: New Anticonvulsant in the Treatment of Epilepsy, 3-Methyl 5,5-Phenylaethylhydantoin (Hydantal): Preliminary Report, Northwest Med. 44: 210 (July) 1945.

## Special Article

# MEDICAL CONDITIONS IN ALASKA

### A Report by a Group Sent by the American Medical Association

HARRY E. BARNETT, M.D.
JACK FIELDS, M.D.
GEORGE MILLES, M.D.
JOSEPH SILVERSTEIN, M.D.
and
ARTHUR BERNSTEIN, M.D.
Chicago

The advisory committee of the American Medical Association to the Department of the Interior appointed a team to study the over-all medical conditions and problems of the territory of Alaska and to render such special advice and aid as could be given.

Alaska was toured for a period of three weeks. The team arrived in Anchorage July 19 and completed its tour on August 9. The following sites were visited: Anchorage, Seward, Bethel, a native village on the Kuskokwim River, Unalakleet, Nome, Gambell on St. Lawrence Island, Kotzebue, Point Barrow, Tanana, Fairbanks, Juneau, Hoonah, Sitka, Ketchikan and Metlakatla. A total of about 4,500 miles was traveled in Alaska.

The team was capably guided by Dr. C. Earl Albrecht and Dr. Leo Gerhig of the Territorial Department of Health and Dr. Howard Rufus of the Alaska Native Service. Physicians of the Alaska Native Service, as well as private practitioners, were consulted as to their problems. Nurses in the field, at Alaska Native Service hospitals and at private hospitals were interviewed. Local officials such as village mayors and councilmen as well as territorial officials were interviewed. A conference was held with Gov. Ernest Gruening.

School facilities were examined and school teachers were interviewed, as they are an important cog in the health of the small isolated communities in Alaska. Statistics on venereal disease were examined, and the military, health officers and private physicians were interviewed. Patients were examined and treatment or suggestions for management were offered. The team performed several operations and examined several hundred patients. The number of places visited and the distances covered gave the team an excellent insight into the situation regarding the over-all medical picture in Alaska.

Alaska is 586,000 square miles in area, or one fifth the size of the United States. It is twice as large as Texas. Distances are greater than many anticipate; the distance from Ketchikan in southeastern Alaska to Attu, westernmost of the Aleutian Islands, is greater than that from New York to San Francisco. From Ketchikan to Point Barrow the distance approximates that from Seattle to the Mexican border. The size of Alaska is readily appreciated by noting the extent of a map of the territory superimposed on a like-scale map of the United States.

The greater part of the northwestern portion of the territory (north of the Alaska Range) has "permafrost," or permanent frost; this is a condition of permanently frozen soil from within a few inches of the surface down to bed rock, several feet to many hundred feet into the earth. This condition hampers the laying of pipes for

water supply and sewage disposal, which is such an important feature for proper sanitation and hygiene. The climatic condition of the territory is characterized by low temperatures in the interior (minus 70 F.) and an extremely short growing season in the summer. The territory has not been widely developed from an agricultural standpoint, and food as well as dairy products are imported with resultant high costs of these products.

The present population of Alaska is estimated to be between 90,000 and 100,000; of these 32,000 are natives. The native population has remained unchanged since the purchase of Alaska in 1867. The natives consist of about 15,000 Indians and 15,000 Eskimos and 1,200 Aleuts. The nonnative population has increased since the onset of the war and has continued to increase with the opening of the Alcan Highway and the influx of workers hired by contractors for War and Navy Department activities progressing at this date. The population of Anchorage has grown from 3,400 to 10,000 during the war years, and this trend has continued; hence, an accurate estimate of the population cannot be made. All other cities in Alaska have increased in population, though to a lesser extent; Juneau, Fairbanks, Sitka and other cities have increased about 50 per cent over their prewar census.

Defense of the continental United States, in fact of the whole North American continent, has become a very pertinent factor with regard to Alaska, which has been called the "left flank of the North American Continent." Its strategic position is being emphasized by the recent world unrest. A healthy populace as well as a stable increase of the population of the territory would aid in the defense of Alaska. The territory is also being used for arctic training of the troops, a site which cannot be equaled under the American flag. Again, a healthy populace would reflect on the health of members of the armed forces, as they would then not be exposed to communicable diseases.

### TUBERCULOSIS

Tuberculosis constitutes the most urgent and important health problem in Alaska. The statistical data are unassailable, and these with our personal inspection served to impress the committee with the urgency of the problem. In discussions with many private practitioners, physicians of the Alaska Native Service and the territorial health commissioner the problem was emphasized.

Pulmonary tuberculosis was seen at every activity visited. A half day was devoted to the examination of patients in the outpatient clinic at Bethel. Six new cases of open tuberculosis were observed, but the patients had to be sent home because of the lack of facilities for their care. Dr. Langraam, Alaska Native Service physician at Bethel, stated that regardless of the presenting disease 50 per cent of cases were complicated by tuberculosis.

Extrapulmonary tuberculosis was seen to occur in an unusual proportion of the population. These infections consisted of bone and glandular involvement. Cases of tuberculosis of the spine in both the active and inactive stages were a common sight after a short stay in the territory. Many of the extrapulmonary lesions were accompanied by pulmonary involvement, and this complicated the problem of treatment. The majority of the crippled children in the territory had tuberculosis of the bone, as revealed by a recent survey.

The death rate from tuberculosis of 359.1 per hundred thousand for the year 1945-1946 is probably among the highest in the world. The rate for the United States was about 40.1 per hundred thousand. The Alaskan rate is nine times the rate in the states. The native rate is much higher than the over-all rate indicates—perhaps fourteen times the over-all rate in the United States, while the rate for the white population is twice as high as in the states. In the states the over-all death rate from tuberculosis includes the high incidence among the Negro and Mexican segments of the population. It is also common practice among the white population in Alaska to go "outside" for treatment of tuberculosis when the diagnosis is established. (The term "outside" refers to the United States.) The rate, therefore, is not padded by any unusual circumstances but reflects probably a lower trend than is actually true.

The total number of cases of open pulmonary tuberculosis in Alaska approximates 4,500. This figure is arrived at by the usual practice of multiplying the number of deaths from tuberculosis by nine to arrive at a conservative figure of open cases. Incidence in some villages has been established as 25 per cent of the population of the village by recent mass survey statistics.

About 60 per cent of the cases of tuberculosis reported to the health department in 1945 were first reported on the death certificate. This means that in Alaska during 1945 over half of the cases discovered were unrecognized until death. This figure dramatically points to the need of additional efforts at control.

When deaths from tuberculosis are compared to deaths from all causes, including injury, organic disease and suicide, it is found that tuberculosis causes one of every five deaths, or in other words accounts for 20 per cent of the mortality in the territory. The analysis of deaths due to communicable disease in Alaska for 1945 reveals that 69 per cent of all such deaths were due to tuberculosis.

Dr. Rabeau at the Alaska Native Service Hospital in Kotzebue had compiled some decidedly interesting statistics from his records. Kotzebue is a village of 1,200 persons, all Eskimos. For a period of four and one-half years the death rate in this community was 3,600 per hundred thousand. Of these deaths 54.7 per cent were directly the result of tuberculosis, the diagnosis having been proved by autopsy in over half the cases. Dr. Rabeau reported that in a period of seventeen months he cared for 40 patients with tuberculous meningitis. It was his opinion that 25 per cent of all the natives in the community which he served had open tuberculosis, a figure that has been substantiated in several communities by the mass roentgenologic survey now in progress. He further estimated that an additional 35 per cent of the natives had what he would be willing to classify as arrested tuberculosis.

The school teacher at Barrow stated that of 30 children between the ages of 5 and 6 who had entered school but 6 lived to finish. The majority of deaths were due to tuberculosis.

The *M/S Hygiene,* the Territorial Health Boat, reported on a visit in 1945 to Perryville, a village of 70 persons, that there were 7 patients who had far advanced tuberculosis with positive sputums. As a result of this high incidence of active tuberculosis the infant mortality was extremely high. More than

one half of the children born in this village died before they were 6 years of age.

The high rate of tuberculosis among the natives can be ascribed to many factors. The natives may have a lower resistance than those of the white race. However, contact is probably the most important factor. In the native villages housing, in the vast majority of instances, is very poor. As many as eleven persons were found living in a single room about 9 by 12 feet, with little ventilation. It is evident that the presence of an open case of tuberculosis would expose all members of the group to large and frequent doses of tubercle bacilli. Furthermore, the native is rather stoical and only infrequently presents himself for medical care in the absence of urgent symptoms, among which he has come to recognize that spitting of blood is especially ominous.

The committee was surprised to learn that up to the spring of 1945 no sanatorium for the treatment of tuberculosis existed in Alaska. Patients, when the case had been diagnosed as tuberculosis, were either sent back home to be cared for by their family or kept in an Alaska Native Service hospital. The latter amounted to custodial care only. The facilities in Alaska up to 1945 totaled a maximum of seventy beds in Alaska Native Service hospitals, and these were for native beneficiaries only. White or nonnative beneficiaries are not cared for by these facilities except in emergencies.

Since 1945 two separate facilities have become available for the treatment of tuberculosis; the sanatorium on Alice Island, Sitka, and the Seward Sanatorium, a total of two hundred and fifty beds. Both of these are reconverted army hospitals of temporary construction. The first is an Alaska Native Service facility, while the latter is a territorial facility leased to the Methodist Mission for management.

The Seward Sanatorium depends on territorial funds, Veteran Administration funds while veterans are hospitalized and Alaska Native Service funds for hospitalized native beneficiaries. The Seward Sanatorium must maintain a hundred and twenty-five bed capacity to be financially sound. While we were in Alaska the Alaska Native Service was forced to withdraw its financial support from the Seward Sanatorium because a deficiency appropriation to cover the native patients in the Seward Sanatorium did not pass in Congress. This last fact struck the committee as a thunderbolt, as it now appears that the Seward Sanatorium has been virtually scuttled.

The existing sanatorium facilities are hopelessly inadequate to stem the tide of tuberculosis. The problem at present is selection of the few patients for admission from the many whose cases have been uncovered, since the number of beds is so limited. Many cases are far advanced and hopeless as to prognosis. The occupancy of a bed by a patient whose case is hopeless seems unfair when perhaps 10 or 12 less seriously ill patients whose disease is more amenable to treatment are awaiting admission. Of course, the hospitalized patient in the hopeless case is at least removed from his family and the public and so does not serve as a disseminator of the disease.

In each Alaska Native Service hospital a few beds are provided for the care of tuberculosis. These are general hospitals, and where a physician is in residence, as at Kotzebue, Bethel and Juneau, tuberculosis patients were in good proportion to the total number of beds. In hospitals that did not have a resident physician the bed capacity was not utilized and tuberculosis patients were not in adequate proportion to the occupied beds. The latter was true in such places as Barrow and Tanana. In the general hospitals of the Alaska Native Service treatment of tuberculosis amounts to custodial care for the most part, and only at Bethel and Juneau were pneumothoraces performed.

The case finding program of the Territorial Department of Health is progressing very satisfactorily. Three separate equipments are being utilized. First, the *M/S Hygiene,* the Territorial Health Boat, travels Alaska's shoreline calling at isolated villages from Ketchikan and Metlakatla to Nome. This work is continuing and will be a year round project of the Department of Health. Second, a 4 by 5 General Electric 200 milliampere photofluorographic unit is being transported from one large city to another in the territory. This unit was operating in Anchorage when the committee first arrived in Alaska. This unit will continue its circuit throughout the larger cities of the territory, including Palmer, Fairbanks, Nome, Unalakleet and possibly Bethel, Seward, Kodiak, Juneau and Sitka. When this itinerary is completed the residents of all cities of a population greater than 1,500 to 2,000 will have been examined. Third, the Mobile Health Unit, an army small arms repair truck, is equipped with clinic facilities, health education materials and a 30 milliampere portable Picker X-Ray machine. This mobile unit serves the highway system of the territory.

The last method of roentgen examination of territorial residents is through the private physicians and hospitals. The Territorial Department of Health pays $2.50 and furnishes the film for any roentgenogram taken on persons suspected of having tuberculosis. This program resulted in approximately 3,000 roentgenograms during the past year, all of which were interpreted at the Juneau office.

Further plans for case finding include the use of a 30 milliampere portable Picker Field Unit, which can be transported by plane in smaller communities. These communities cannot be reached by road, rail or boat. It is in these smaller villages that the incidence of tuberculosis is high.

The after-care and rehabilitation of tuberculosis patients is almost a nonexistent project in Alaska. Territorial funds were appropriated during the special session of the Territorial Legislature in 1945 for such a program to be operated under the Social Security Agency. A subsequent appropriation for this program at the 1946 legislative session was totally inadequate to carry out the intent of this program. At present the only effort at rehabilitation possible will be made with the aid of the limited funds available from the Alaska Tuberculosis Association. These will consist in a wholly inadequate program of occupational therapy and organized amusement of patients in the sanatoriums.

A central case registry for tuberculosis has been started in the Juneau office of the Territorial Department of Health. It has been indicated that the registry will be divided, in that all cases from the interior of Alaska will be filed in Anchorage. This will facilitate the management of the control problem in the interior.

The committee saw a number of patients with open cases housed in 9 by 12 foot rooms among eight to twelve persons, all members of one family. Can isola-

tion be practiced in such homes? Is it a wonder that the life expectancy of the natives is so short? The Barrow school teacher's statement tells the story; he said: "Of a class of 30 that entered school, 6 have lived to graduate." Is it a wonder that the total native population of Alaska has not increased from what it was when the territory was purchased in 1867?

Tuberculosis is a preventable disease. The white plague can be controlled in Alaska and in a period of five to eight years the death rate and incidence need not be greater than in the best areas in the United States.

For those who decry federal aid the committee wishes to point out that the problem in Alaska has existed for many, many years without even an effort toward a solution until 1945. The territorial funds are insufficient to meet the present needs of Alaska in tuberculosis control. Alaska has been a neglected possession of the United States up to recent years. The war years and its present eminence as the "left flank of the North American Continent" have brought Alaska into the national conscience. The citizens of Alaska, its officials and the health authorities are cognizant of the acute problems. Defense of Alaska would best be accomplished with a healthy populace.

In the face of the serious tuberculosis problem in Alaska, Congress has seen fit to reduce the already meager funds of the Alaska Native Service for the care of the tuberculous. It must be emphasized to those who may be color or race conscious that the tubercle bacillus knows no color line. To those who measure in terms of tax dollars it must be evident that in a course of years inadequate attempts at control of tuberculosis is wasteful. To the industrialist and employer who think in terms of production, it must be pointed out that a labor market grossly infected with tuberculosis is an economic liability. To the military who are prone to think in terms of effective fire power the ever present danger of tuberculosis is both a direct impediment to the efficiency of their forces and a demoralizing factor. Finally, to the parents, relatives and friends of those going to Alaska, both as civilians and in armed forces, the rate of tuberculosis in the territory constitutes an ever present danger.

### EYE HEALTH SURVEY

The Eye Survey was carried on at all localities visited. About 50 to 60 natives were examined in each village. The total number examined was well over 600. The persons were taken at random, and the majority were children. The greater part of the study was among the Eskimos.

Early in the course of the tour it became evident that corneal opacities among the Eskimo natives were extremely prevalent. These lesions were a result of acute processes in the early years of their life, and later the resultant scars caused poor vision. The universal distribution of corneal lesions among the villages of arctic Alaska was striking.

The ocular pathologic processes noted in order of frequency were phlyctenular keratitis (inactive), phlyctenular pannus (active), phlyctenular keratitis (active), phlyctenular conjunctivitis (active), chronic conjunctivitis (cause undetermined), angular conjunctivitis (cause undetermined), squamous blepharitis and phthisis bulbi. Many cases of convergent strabismus were seen. In the older age group senile cataracts in the various stages of progression were noted, some of them in need of extraction.

The observations revealed that from 22 to 50 per cent of the children examined in any village exhibited corneal opacities. Some villages had a higher incidence than others. These opacities varied from pinhead-sized infiltrates, nebulous in character and not interfering with vision, to large dense leukomatous opacities causing a decided reduction in vision. All parts of the cornea seemed to be involved. The consequences of these corneal lesions are reflected in the following observation: of the 600 persons examined, 40 had corrected visual acuity of 20/100 or less. This figure is referred to as "industrial blindness."

Coincident with this committee's tour, an ophthalmologist employed by the Territorial Department of Health under the auspices of the Vision Conservation Program was just completing a six weeks' study. In comparing the statistics of the various ocular diseases it was found that the observations were similar. Independently the opinions agreed as to the probable causes and management of these conditions.

It is considered that there is no association between the corneal lesions and trauma, malnutrition, tuberculosis, exposure or actinic rays. The causes of the corneal opacities were not determined in this survey. The opportunities for etiologic studies could not be used to advantage in a short visit. The contributing factors of these corneal involvements can be listed as follows: (1) poor personal hygiene, which permits the growth of the staphylococcus or other organisms; (2) totally inadequate medical facilities for diagnosis and treatment in children between birth and 5 years of age, when these corneal lesions occur, and (3) the lack of knowledge on the part of the physicians, nurses, school teachers and parents as to the connection between the "sore eyes" of infancy and the corneal opacities of later childhood and adult life. An interesting observation was made at Gambell, St. Lawrence Island. Here 50 children were examined and only 2 instances of corneal opacities were noted. It proved that these 2 children had been adopted from Nome and had come to Gambell recently. It is in Gambell that the school includes showers every Friday as part of the school curriculum.

Alaska does not have a qualified ophthalmologist. Numerous cases require surgery. Many patients with corneal opacities would be benefited by corneal transplants. Refractions for the presbyopic persons to aid them in carrying on their occupations are not available in small communities.

The ophthalmologist of this team performed the following surgical procedures: strabismus cases, 2; enucleation, 1, and cataract extraction, 1.

### VENEREAL DISEASE

Venereal disease is one of the serious medical problems of the Territory of Alaska. The problem is especially serious in the larger cities, where recent increments of population have occurred due to defense work. The areas are usually in close proximity to military posts, and the incidence of venereal disease among the military personnel is unusually high. This latter is true in such places as Fairbanks and Anchorage.

The biennial report of the Office of the Commissioner of Health for the period July 1, 1944 to June 30,

1946 revealed a decrease in the incidence of syphilis but an increase in the incidence of gonorrhea during the fiscal year 1945-1946 as contrasted with the year 1944-1945. This report included venereal diseases occurring in military personnel. Since many troops left the territory during the latter part of the reported period, it is evident that the increase of gonorrhea is definitely significant.

Many factors contribute to the present incidence of venereal disease. Among these may be included alcoholism, the "line," the preponderance of male over female inhabitants and the rapid expansion of population due to defense activities.

Alcoholism plays an important role in spreading venereal disease. General Everest, the commanding officer of Ladd Field, informed this group that most of the soldiers infected stated that they had been intoxicated at the time of exposure.

In Fairbanks the community condones open prostitution. "The line" extends along Fourth Street, in the very heart of town. Twenty-three inmates of this street openly solicit and are unmolested. Control of venereal disease cannot be accomplished under these circumstances. Community indifference and outmoded ideas of "family protection" are the most important reasons for the existence of the professional prostitutes. Financial gains to the property owners may be another reason.

The Territorial Department of Health has been making a concerted effort to combat venereal disease. It has distributed literature to the physicians explaining in detail the accepted modern modes of treatment of venereal disease, and it has furnished without charge diagnostic and therapeutic measures for control of venereal diseases.

Several physicians in private practice who were interviewed said that they were prevented from completing a course of antivenereal treatment in indigent patients because of lack of medicaments. The commissioner of health, Dr. C. Earl Albrecht, explained that there were no funds available for further purchases of drugs.

The Territorial Department of Health received $24,200 of venereal disease funds for the fiscal year of 1948. A considerable amount of this must be applied to the support of four laboratories: Ketchikan, Juneau, Anchorage and the *M/S Hygiene*. A relatively small amount goes toward administrative and nursing budgets and the remainder to direct venereal disease control measures. It is wholly inadequate to curb the spread of gonorrhea and syphilis. Fortunately, however, a grant of $7,000 from the U. S. Public Health Service for the rapid treatment of syphilis was received recently. This will help, but additional funds or their equivalent in personnel or drugs for other venereal control measures is needed.

The reason Alaska gets only $24,200 is the injustice of the allotment system. Ninety thousand persons are spread out and are overburdened with literally tens of thousands of troops and construction workers for rehabilitation, defense and civilian construction. Alaska has the need for intensive venereal disease control assistance by the U. S. Public Health Service. The tragedy is the spread of venereal disease to isolated native groups who were clean in the past and now have been infected and have taken it back to their homes and communities. It is simply getting out of control.

At present the venereal disease program is administered by the territorial commissioner of health under the Division of Communicable and Preventable Disease Control. This is a weak link in the chain of control. The commissioner of health has so many duties, the most important being administration and organization of his department, that the Division of Communicable and Preventable Disease Control suffers as a result. A separate person should be in charge of the Division of Communicable and Preventable Disease Control. The function of this division is an exceedingly important one, not only as regards venereal disease control. The U. S. Public Health Service should supply the director as well as sufficient financial aid to assist Alaska in its fight against venereal and other communicable diseases. The problems exist because of recent increases in the population, mostly transients, and as a result of defense activities in the territory. The problem of venereal diseases among the military makes it one for federal subsidy.

### COMMUNICABLE DISEASES

Communicable diseases, other than tuberculosis, are an ever present threat in Alaska. The danger is aggravated by the recent increase in population due to defense work, Alaskan Railroad rehabilitation program, dependents of the armed forces and transients. The general substandard sanitation and housing facilities that exist throughout the territory make the problem an urgent and potentially dangerous one. It is surprising that serious outbreaks of diseases have not occurred.

The committee was informed of a current outbreak of typhoid in two separate areas of the territory during our visit, July 1947. Four proved cases occurred in the village of Nenana and 3 cases at Anchorage. Nenana has no hospital facilities, while at Anchorage the hospital facilities are inadequate for the community and there are no isolation beds.

The committee was impressed with the fact that none of the existing hospital facilities provide beds for the isolation of communicable diseases. During an epidemic of diphtheria in Anchorage in August 1946, 35 patients were isolated in a quonset hut.

Alaska has many ports through which diseases may be carried into the territory. The rat population of many of these ports is in such proportion as to make plague a real threat.

All the exanthems as well as influenza and enteric diseases have been reported in the territory each year. Measles, diphtheria and influenza have occurred in epidemic proportions. Tularemia and trichinosis have occurred, though not in serious numbers. An epizootic of rabies has occurred along the Yukon and Kuskokwim River areas, and its greatest severity was manifest along the upper region of this drainage. No human cases of rabies were reported, but several persons were given the Pasteur treatment as a precautionary measure when they reported that they had been attacked by animals displaying symptoms of "madness."

International travel through Alaska is expanding rapidly. Regulations, appropriations and personnel should be provided for this.

### SANITATION

Sanitation and engineering is a division of the Territorial Department of Health. The sanitation and engineering program is comprised of education, inspection,

consultation and enforcement services to the public and to persons on the subject of sanitation in the following fields:

1. Water supply
2. Sewage disposal
3. Food handling
4. Milk supply
5. Salmon, clam, crab and shrimp processing
6. Practice of cosmetology and barbering
7. Operation of hotels and rooming houses
8. Garbage collection and disposal
9. Housing
10. Swimming pool and bathing beach construction and operation
11. Interstate carrier watering points
12. Bottled waters and beverages
13. Water pollution
14. Plumbing
15. Heating, lighting and ventilation of dormitories, schools and public buildings
16. Rodent control
17. Industrial hygiene
18. Property and public health nuisances; requests for advice from private individuals, and requests for advice from local health officials.

The application of principles of basic sanitation was among the first organized public health endeavor in Alaska and started about eleven years ago. In spite of progress, much still remains to be done if the environmental sanitation of Alaskan communities is to meet reasonable standards.

Personnel problems in the Division of Sanitation and Engineering have been very trying in the past few years. Unsettled war and postwar conditions, combined with the high cost of living in Alaska and housing problems, were doubtlessly the cause for a great turnover. During the greater part of the biennium of July 1, 1944 to June 30, 1946 there were two or three professional employees and two clerical employees. This situation has not improved since these dates. Seven different professional employees and seven different clerical employees were on duty with the division during the biennium July 1, 1944 to June 30, 1946. The services of four of the seven professional employees who were on duty with the division were loaned to the Department of Health by the U. S. Public Health Service during the above reported biennium. The division staff has been limited to two or three professional employees during practically all of its existence, and few of the personnel have remained over a year or two.

The facts regarding personnel emphasize the inadequacy of the solution of the sanitation problems, especially in view of the extensive list of duties of the Division of Sanitation and Engineering, as previously mentioned.

The difficulties that confront work in sanitation and engineering in Alaska are those of geography and climate. The great distances between inhabited points and the difficulty in reaching these places become self evident when the map is consulted. Climate, especially in the arctic, is an ever present hazard and problem. Permafrost exists in the entire arctic region; in winter the earth is solidly frozen up to the surface with concomitant external temperatures of minus 70 F. One can easily visualize the difficulties in laying water and sewer pipes.

The committee saw at first hand the problem that exists in Nome. Water is piped into the homes and business places during the summer, for a period of three months. At all other times it is purchased in gallon quantities from carts and water wagons. The sewage condition is much worse. No flush toilets exist in Nome except on the street facing the ocean beach. The toilet facilities consist of simply a bucket, and a crew of pick-up men making the rounds at intervals. The latter is referred to as "the honey wagon." The situation would be humorous, with the stories of frozen buckets in winter, if it were not so serious. The city of Nome, either because of finances or inertia of its citizens, has not been able to solve its sanitation problem.

Public sewerage and sewage disposal methods were inspected in most of the principal towns and in many small villages and outlying areas. These inspections disclosed the continued improper discharge of community sewage on tidal flats, in small streams and on beaches in most of the coastal towns.

In the biennial report for the period July 1, 1944 to June 30, 1946 a careful study of known conditions of three significant features of sanitation—public water supply, public sewage and garbage disposal—are reviewed. Existing conditions were compared, community by community, on a percentage-of-adequacy basis, with recognized standards of good United States practice. While it was evident that much improvement in basic sanitation is needed, many communities, such as the villages of arctic Alaska, cannot economically provide all the protection and conveniences of year around, citywide water and sewer systems.

*Average Per Cent Adequacy of Sanitation Facilities*

| Judicial Division | Water Supply, % | Sewerage, % | Garbage Disposal, % |
|---|---|---|---|
| I Southeastern | 59.0 | 38.0 | 29.0 |
| II Arctic and Bering Coastal | 2.5 | 0.5 | 3.0 |
| III Southern Pacific Coastal | 22.0 | 18.0 | 17.0 |
| IV Interior | 7.5 | 11.0 | 10.0 |
| Entire territory | 30.0 | 20.0 | 17.0 |

The data in the accompanying table show clearly the great need for major improvements in public water supply and sewerage systems.

The committee was impressed with the vast duties of the Division of Sanitation and Engineering, and discussions with the health authorities emphasized this. As an example it may be cited that there are four hundred canneries in Alaska. It is difficult to conceive that all of these are properly inspected during the short season in which they operate.

## PERSONNEL

The problem of attracting well trained persons into the territory to fill the needs of all specialized fields is an extremely important one at this time. The Territorial Department of Health and other agencies dealing with health, such as the Alaska Native Service, have difficulty in filling positions. The efficiency of government throughout the territory is being seriously impaired by the lack of personnel. The annual turnover among federal agencies in the Anchorage area varies from a low of 35 per cent in the Civil Aeronautics Administration to 120 per cent in the War Assets Administration. The average term of employ-

ment in the Territorial Department of Health is nine months. The weather bureau, the Alaska Railroad, the school system and most other agencies face the same problem.

Personnel problems in the Division of Sanitation and Engineering have been very trying in the past few years, as has previously been stated. The Territorial Department of Health, as well as the Alaska Native Service, has unfilled positions for physicians. The resultant lack of medical care reflects on the over-all health condition of the territory. The reasons for the personnel problems can be attributed to the following factors: high cost of living in the territory; isolation of the individual in remote communities away from professional contacts, and, finally, the housing shortage.

The high cost of living is attributed to the fact that most of the food and all other commodities are imported from the states. Freight and shipping rates added to the cost of a moderately priced item of food, clothing, utensil or furniture results in a sizable increase over the price in the states.

The wage differential for employees of the territory is not remarkable. Salaries for employees of the Territorial Department of Health are similar to those in the states for comparable positions. Salaries of employees of the U. S. Public Health Service assigned for duty with the Department of Health have a 10 per cent differential for "overseas" pay. Civil service employees of the Department of the Interior, of which the Alaska Native Service is a division, have a 25 per cent differential in salary for service in Alaska.

Unskilled workers as well as those skilled in trades in Alaska receive unusually high salaries on the open labor market. The territory is at a decided disadvantage in competing with this market. The committee was informed that two employees of the Division of Sanitation and Engineering had resigned recently to accept positions as policemen in Fairbanks.

Isolation, especially of a physician, in remote villages in Alaska for an indefinite period is a deterrent in attracting capable men. Professional contacts do not exist. Facilities for postgraduate training have not been provided. In order to obtain postgraduate training a physician would have to return to the states and extend his leave of absence at his own expense.

Housing shortages without any doubt are the chief deterrent to the encouragement of permanent residence in the territory at the present time. Families have come to the territory with a good job and adequate finances but after weeks or months in a hotel room have given up in despair and returned to the states. Efforts of such governmental agencies as the Alaska Railroad, War Department and Civil Aeronautics Authority to provide housing for their employees are commendable. However, the health agencies have not been as active in providing abodes for their employees. Alaska Native Service hospital facilities at Tanana and Kotzebue are without housing for a physician and his family.

## HOSPITALS

The following hospitals were inspected by the Committee:

*Anchorage*

The Provident Hospital is a modern fifty-five bed fire-resistant building with extremely modern equipment. It is well staffed and well furnished. It is by far the best hospital physical plant visited. It is run by a Catholic order of Sisters.

*Seward*

The Seward General Hospital is a small one and one-half story wooden structure, a single room being used on the second floor. It is old and appears to be in a rather poor state of repair and is overcrowded. It is distinctly a fire hazard. The Methodist Board operates this hospital.

The Seward Sanitarium is an army hospital taken over by the Territorial Health Department and leased to the Methodist Board. It is a temporary army hospital of unit type, one story, wood construction and with adequate fire breaks and fire protection. It appears to be well equipped and in a good state of repair. This type of construction is expensive to maintain.

*Bethel*

This Alaskan Native Service hospital is a two story, thirty-six bed wooden structure in excellent physical repair. There is considerable overcrowding as indicated by the fact that a few pediatric patients were in wheelchairs. The equipment is good.

*Nome*

The Maynard Columbus Hospital, operated by the Methodist Board, is a two story wooden structure. The building is old, in a poor state of repair, and has a decided list due to the settling of the foundation. The main stairway to the second floor is narrow. The building is a fire trap. It should be replaced before a serious catastrophe occurs.

*Kotzebue*

This Alaska Native Service hospital is an old, two story, thirty-one bed wooden structure in a good state of repair. It was overcrowded.

*Barrow*

This Alaska Native Service hospital is a two story, eighteen bed wooden structure, comparatively new, well equipped and designed.

*Tanana*

This Alaska Native Service hospital is a two story, thirty-three bed wooden structure, comparatively new, well equipped and designed. No facilities for living quarters for a physician are provided.

*Fairbanks*

The St. Joseph Hospital is a three story, asbestos-shingled, wooden-framed building, comparatively modern and relatively well equipped. It is conducted by a Catholic order of Sisters. It appears to be rather crowded.

*Juneau*

The Alaska Native Service operates a two story frame hospital. It is a general hospital with a few beds for tuberculosis. Because of lack of funds it is being reduced to fifteen beds.

The general hospital is frame and concrete. It appears to be in a good state of repair. It was not given a detailed inspection.

*Sitka*

There is no public hospital in Sitka. The local population depends on the beds in the Pioneers' Home. This facility is made available with some reluctance on the part of the authorities, and while this building is of excellent and fireproof construction and the hospital section is well equipped, it does not appear to meet the needs of a community of this size. Obstetric cases are delivered in the Salvation Army Home.

*Alice Island—Sitka*

The tuberculosis sanatorium is a temporary army hospital of single story units, wooden construction, and adequately protected from the hazard of fire. It appears to be rather well equipped.

The Orthopaedic Hospital and Mt. Edgecombe Infirmary: These two units are housed in a permanent, semifireproof, two story building constructed by the Navy. The physical plant and equipment are superior.

*Ketchikan*

The general hospital is operated by a Catholic order of Sisters. It is a three story frame and concrete building in a good state of repair. It is something of a fire hazard.

The general hospitals of the territory are grossly inadequate to meet the medical needs of Alaska. In all but one of the sites visited (i. e., Ketchikan) the hospitals were inadequate from the point of view of bed capacity and in most places the physical plant was also inadequate. The insufficient hospital facilities can be attributed to the rapid growth of the population in the larger cities of Alaska as well as the fact that civilian hospital construction has lagged during the past several years. The causes for the latter are the same as for the shortage of housing in general, namely, scarcity of materials and high building costs.

Most of the hospitals surveyed were wooden, and the committee was impressed with the fire hazard that these buildings presented. Indeed, it was reported that two hospitals had burned in the past year. These hospitals were at Palmer and Valdez, and the communities are now without any hospital facilities. The hospital at Nome (Maynard Columbus) gave the impression of "a tragedy waiting to happen."

The general cost of hospital construction in Alaska is appreciably greater than in the states and is probably more than 50 per cent higher per bed. The per bed cost of construction decreases up to a certain point with hospitals of increasing bed capacity. A fifty bed hospital is more expensive to construct per bed than a two hundred bed institution. This is because certain of the utilities, such as heating plant and laundry, are inherently the same for a small as for a large hospital.

The Hospital Survey and Construction Act has provided funds to states or territories in which a comprehensive study has resulted in the formulation of an acceptable and coordinated hospital plan. Alaska has complied with this requirement. The Hospital Survey and Planning Unit of the Territorial Department of Health is under the administrative direction of the Board of Health.

The allotment to Alaska from the federal government's $3,000,000 fund for survey and planning is $10,000. This is to be matched by territorial funds in the ratio of $2 of territorial funds for each $1 of federal funds. The payment of the $10,000 allotment to Alaska has been made, and the survey is in progress.

The federal fund for hospital construction is $75,000,000, of which $41,400 is available to Alaska. The matching ratio of territorial and federal funds remains 2:1. The federal allotment is based on population and other factors. It penalizes the more thinly populated states and territories, because their need is relatively greater than their ability to match funds.

### MENTAL HOSPITAL

No hospital for the care and study of mental diseases exists in Alaska. Indeed, there is no facility of any type available for mental patients. All persons committed to an institution for reason of mental disease are sent to Morningside, Ore.

The procedure of committing a person to a mental hospital is archaic and bears reporting. Any person may swear out a warrant attesting to the mental ills or incapacity of another. The "suspect" is then placed in confinement in a federal jail for ten days. During this time two physicians must examine the "suspect" and make statements as to their findings in the case. A jury then weighs the facts and signs the commitment papers if the patient is adjudged insane. The marshal then transports the patient to Morningside, Ore.

It should be observed that any citizen may make another a "suspect" only by swearing out a warrant; that the patient is confined in jail; that psychiatric studies are not mandatory and indeed are not possible, as only one physician in the territory practices psychiatry, and that only the marshal has custody of and transports the patient a considerable distance to Morningside, Ore. The marshal usually waits until he has an appreciable number of patients before he makes the trip "outside." Three hundred and ninety patients from the territory are at present confined in the sanatorium in Oregon. The Department of the Interior bears the expense of these confinements on a per diem per patient basis.

### ALCOHOLISM

Alcoholism has assumed the proportions of an important problem in Alaska. In discussing the general and over-all health problems of the territory with physicians, teachers, military authorities and the "man on the street," the subject of alcoholism was always spontaneously referred to by them.

Alcoholism can rightly be classified as a disease. It accounts for a great deal of human suffering to both the victim and his dependents. Indigency, venereal diseases, poor housing, poor nutrition and general poor health can be attributed directly or indirectly to alcohol.

Alaska has been cited to the committee as having a larger per capita rate of alcohol consumption than any state.

The native does not appear to tolerate alcohol as well as the white man. In villages where alcohol was not permitted it was observed that housing and the general conditions were very good. The natives of these villages were well clothed and were better nourished. In villages where alcohol was sold the situation was quite reversed. It became easy, after a while, to determine from casual observation of the village whether alcohol was or was not a problem.

### HOUSING

The acute housing shortage in Alaska enters into every phase of a discussion about the territory. Personnel problems in every governmental department as well as in private industry are related to the lack of adequate housing. The whole economy and defense of Alaska hinges on a stable permanent populace, and this is hindered by the housing problem.

Housing has not kept pace with the increase in population. During the war there was a complete restriction on the transportation of building materials for private use. Since the end of the war such factors as freight rates and scarcity of materials and skilled workers have combined to prevent the fulfilment of the need for more housing.

Not only is the quantity of housing appallingly insufficient, but the quality throughout the territory is extremely bad. It can be stated conservatively that 50 per cent of the housing in Alaska is substandard. Hundreds of houses in the coastal towns are built on piling over tidewater, and many have large and ancient accumulations of garbage and sewage beneath them. Hundreds of families, particularly in the vicinities of Anchorage and Fairbanks and along the highway, are living in huts, cabins, hovels, tarpaper shacks, tents and trailers. These dwellings are not situated where standardized and supervised facilities for water supply, sewage and garbage disposal exist.

It should be particularly emphasized that the entire situation not only is deleterious to the health of Alaska at present but is fraught with potential dangers for the future.

## SUMMARY

The observations of this committee were essentially in agreement with the opinions previously expressed by the health authorities and other interested persons in the Territory of Alaska. The committee's tour of three weeks was a fairly comprehensive one, as the territory was traversed for a distance of 4,500 miles and all important parts, with the exception of the Aleutian chain, were visited. All facilities were made available to the committee, and these, with personal inspections, examination of patients and interviews, rounded out the perspective.

It must be evident immediately that the medical problems of a community the size of the Territory of Alaska are numerous and diverse. The climatic conditions and the lack of adequate transportation facilities serve to accentuate these problems.

*Tuberculosis.*—This is the most serious and urgent problem which faces the territory at present. The death rate is nine times greater than that of the United States. Facilities for the isolation, medical treatment and rehabilitation of tubercular patients are grossly inadequate. The recent removal of government financial support from one of the two available sanatoriums has seriously hampered the existing hospital situation. Alaska is an important cog in the defense of the United States only if its inhabitants are healthy. This is a problem which concerns the federal government and, as such, sufficient federal funds must be made available for its solution.

*Eye Health.*—Ulcers of the cornea and the resulting opacities with poor vision are widespread among the natives. The causes have not been determined and bear investigation. No ophthalmologist resides in the territory.

*Venereal Disease Control.*—The problem of venereal disease is becoming increasingly serious. Organized prostitution and alcoholism together with the rapid increase of population, both military and civilian, have been contributing factors. There are insufficient funds available for adequate treatment, especially among the indigent, and for an urgently needed venereal disease educational program.

*Communicable Diseases.*—The situation with regard to communicable diseases here is potentially very dangerous. Poor sanitation, inadequate housing and a rapidly expanding population are factors which breed epidemics of an explosive nature. No facilities exist for the isolation of patients with communicable diseases.

*Sanitation.*—Sanitation is very poor throughout Alaska, but especially so in the arctic regions where permafrost creates additional problems. Local communities have been unable adequately to establish a satisfactory water supply or sewage disposal system. The Territorial Division of Sanitation and Engineering is handicapped by serious personnel problems.

*Orthopedics.*—The principal cause of deformity and disability of the musculoskeletal system in persons in Alaska is tuberculosis of the bones and joints. The acquisition of Dr. Phillip H. Moore to head the orthopedic hospital at Sitka has been a great step forward in the care of these cases. A second orthopedic center at Anchorage to provide for 75 patients would probably be able to care for all additional orthopedic cases requiring hospital treatment.

*Personnel.*—Three main factors have deterred persons from accepting and holding positions in the territory. These are the high cost of living, the housing shortage and the isolation in remote communities.

*Hospitals.*—General hospitals are grossly inadequate to meet the current medical needs of Alaska, and if a sudden emergency were to arise the situation would be catastrophic. Again this is the result of a rapidly increasing population and a wartime lag in construction. Two hospitals have been recently destroyed by fire and many of the others are potential fire traps. There are no mental hospitals anywhere in Alaska.

*Alcoholism.*—The disease of alcoholism is of sufficient importance in Alaska to be mentioned as a factor contributing to many of the unsatisfactory conditions mentioned in this report.

*Housing.*—There is an acute shortage of satisfactory living quarters throughout the territory. This shortage seriously affects the health and the general economy of Alaska. The solution of the problem should be aided by active federal participation.

## RECOMMENDATIONS

1. *Hospitals.*—There is danger of fire ever present in the presence of wooden hospital buildings. Furthermore, maintenance of wooden buildings is expensive. In spite of their high initial cost, it is urgent that new hospital construction be of a simple, fire-resistant type.

A. Beds for Tuberculous Patients: A minimum of one thousand beds should be provided at once for patients suffering from tuberculosis. This number includes sanatorium beds for the active treatment of tuberculosis as well as isolation units added to present scattered facilities. The isolation units will provide custodial care locally for patients with terminal disease and serve as diagnostic stations. The suggested localities and recommended number of beds are as follows:

Southeastern Alaska: Two hundred and twenty sanatorium beds by expansion of the present facilities at Alice Island.

Anchorage area: Four hundred sanatorium beds. This site is the center of population of Alaska as well as the most easily accessible one by virtue of the Alaska Railroad and highway.

Arctic area: One hundred bed sanatorium in Fairbanks.

Isolation units: Twenty-five beds each in Bethel, Kotzebue, Unalakleet, Fort Yukon and Nome. Government surplus quonset huts or other buildings may be obtained, and the units can be operated as an addition to the present Alaska Native Service or other hospitals.

B. General Hospital Beds:

Replace the hospital facilities at Palmer and Valdez, which have been destroyed by fire.

Build a hospital at Sitka, where the present facilities are makeshift and inadequate.

Replace the hospitals at Nome and Seward before a major catastrophe occurs.

Increase facilities at Fairbanks, Anchorage, Ketchikan and Juneau.

The foregoing recommendations for general hospital beds are made in keeping with the present needs as well as the growing population. The committee is cognizant of the fact that a hospital survey is under way by the Territorial Department of Health as provided by the Federal Hospital Survey and Construction Act. Specific facts and recommendations will result from this survey.

C. Communicable Disease Isolation Facilities: There are no beds for communicable disease. It is recommended that such facilities be incorporated in all general hospitals on the basis of population needs.

D. Orthopedic Beds: Fifty to seventy-five orthopedic beds are needed in the Anchorage area.

E. Mental Hospital: There should be a centrally located mental hospital. One such hospital can provide for the needs of the territory.

F. Anchorage Area: It is recommended that federal agencies and the local community in Anchorage jointly plan their hospital needs in order to eliminate duplication. The committee was informed that there are some forty federal agency offices in Anchorage.[1] The Alaska Railroad has estimated that it requires one hundred hospital beds. Other agencies have a need for and are planning for hospital facilities.

In planning for chronic diseases such as tuberculosis, orthopedics, mental diseases and other chronic conditions, the needs of other than federal beneficiaries must be kept in mind.

A hospital of seven hundred beds, broken down into four hundred for tuberculosis, seventy-five for orthopedics, one hundred for Alaska Native Service general, one hundred for Alaska Railroad general and twenty-five for communicable diseases, is recommended.

2. *Medical Needs for Alaska Native Service.*—A. Hospitals: Present bed capacity of the Alaska Native Service hospitals in the isolated areas is adequate if chronic diseases such as tuberculosis and orthopedics are removed to centers for special care, though each should have facilities for the isolation of communicable diseases including tuberculosis.

All Alaska Native Service hospitals need adequate equipment and maintenance. Critical equipment such as x-ray machines, oxygen units, sterilizers and motor vehicles (ambulances preferred) are needed at all hospitals. The hospital at Kotzebue especially requires a sterilizer and x-ray equipment.

If personnel is to be attracted, living quarters for a physician and his family must be provided at Kotzebue, Tanana and other installations which lack them.

The hospital at Kotzebue should be replaced after more urgent needs have been met.

B. Personnel: There are no physicians at present at Barrow, Tanana and Kanakanak, though appropriations for these positions have been made.

Positions for nurses, dentists and physicians are unfilled, with resultant serious effects on the over-all health problems.

Cognizance should be taken of the extreme isolation of many of the Alaska Native Service facilities. In order to attract desirable medical personnel an attractive employment contract should be set up. It should contain provisions for returning the physician to medical centers, at the expense of the Service, for postgraduate training at intervals of not more than three years.

Recognition of the fact that there is such extreme isolation should result in careful selection of physicians as regards individual adaptability.

Nursing personnel should have a choice of rotation in the different facilities as well as postgraduate training. Their work in isolated hospitals entails more x-ray and laboratory duties than are ordinarily expected of nurses. They should be trained in roentgenologic technic, in the performance of simple laboratory procedures and in anesthesia.

Nonprofessional personnel: Nonprofessional personnel must, of necessity, be drawn from the native population and must be trained in local medical installations. Physicians and nurses should be indoctrinated in this point of view.

3. *Tuberculosis.*—The disease of tuberculosis is prevalent in the native population. It is important to federal interests that the federal government provide a large share of the funds for its control.

A. Case Finding:

The approved methods and present efforts of the Territorial Department of Health toward mass roentgenologic case finding should be enhanced by more federal funds for reasons of the immensity of the problem, transportation costs, defense activities, migrant population from the states, war department workers and dependents of military personnel.

B. Hospitals: Hospital facilities for the treatment of tuberculosis must be greatly expanded. A total of at least one thousand beds is essential. One hundred and twenty-five beds divided into units of approximately twenty-five beds each should be set up in conjunction with the present isolated Alaska Native Service facilities or other hospitals. Suggested sites are Bethel, Kotzebue, Unalakleet, Port Yukon and Nome. The unit would be used specifically for isolation and custodial care of patients with open cases of tuberculosis. These cases can be divided into (*a*) those awaiting transportation to sanatoriums, (*b*) suspect cases under observation for diagnosis and (*c*) those cases that are too advanced to be amenable to active treatment. In addition to present facilities six hundred and twenty-five beds adequately staffed and equipped to permit modern treatment of tuberculosis are required. These should be distributed as follows: One hundred additional beds in southeastern Alaska; four hundred beds in Anchorage, and one hundred beds in the arctic (Fairbanks is the suggested site). Two hundred and fifty beds are in existence at Sitka and Seward.

C. Immunization: It is recommended that an extended immunization program with BCG or a similar method be undertaken among the native population of Alaska.

4. *Eye Diseases.*—The incidence of corneal ulcers is so excessively high that steps should be taken to determine its exact cause in order that prevention and treatment may be intelligently undertaken.

The lack of a qualified ophthalmologist in the territory should be remedied.

5. *Venereal Disease Control.*—Incorporated communities must bring their police codes up to date, and proper enforcement of these codes must be insisted on to aid in the control of venereal diseases.

The federal government should assist the territory in the control of venereal disease. The sudden increase of the population due to defense work, railroad rehabilitation, armed forces in the territory and rapid influx of transient workers has made the problem too large for the territory to handle by itself.

The U. S. Public Health Service should supply the director of the Division of Communicable Diseases, under whose direction the control program for venereal disease as well as other communicable diseases, except tuberculosis, would be adequately supervised.

6. *Sanitation.*—The deplorable conditions of the essential sanitation facilities of all Alaskan communities must be corrected. Local governments have not been able

1. The following are a few of the federal agency offices in Anchorage: Civil Aeronautics Authority; Veterans Administration; Weather Bureau; Alaska Railroad; Federal Bureau of Investigation; Fish and Wild Life; Land Management; Housing Authority; Rural Electrification; Department of Commerce; Post Office; Marine Division; U. S. Public Health Service, and War Assets Administration.

to cope with the problem, which has become acute because of the sudden increase of the population due to defense work, railroad rehabilitation, armed forces' dependents and migrations to the territory. The federal government has a responsibility in the establishment of improved water supplies, sewage disposal units and other sanitation facilities.

The sanitation problems in the arctic have not been entirely solved. The solutions are expensive and require outside assistance.

7. *Communicable Disease Control.*—The control of communicable disease is an increasing responsibility and difficult because of the increasing population. More federal responsibility in funds and personnel must be provided. There is the ever present threat of an epidemic which, if it were to occur, would endanger defense activities as well as the armed forces.

8. *Orthopedics.*—Federal aid to clean up the backlog of orthopedic cases, especially among the children, is urgently needed. The majority of the cases are among federal beneficiaries. Additional hospital facilities, as recommended herein, and professional personnel must be provided.

9. *Public Health Activities.*—The public health activities should be coordinated in that public health should be administered by the official agency (Territorial Department of Health) and hospitalization of federal beneficiaries should be administered by the Alaska Native Service. This may be accomplished over a five year period.

Such public health activities as the work of the *M/S Hygiene* and the mobile units (immunization, education, mass roentgenologic surveys and so forth) have included all elements of the population, but most of the work has been done for the natives. However, any activity of the Alaska Native Service precludes care to white persons or nonnatives.

The Territorial Department of Health is the recipient of federal funds such as tuberculosis control, crippled children and maternal and child health. The efficient administration of these benefits for the whole territory and for all of the population is best accomplished by the coordination of public health activities.

Public health nurses should be a cooperative activity between the Territorial Department of Health and the Alaska Native Service to the benefit of all. Contracts between the two agencies have been executed for such localities as Cordova, Sitka, Wrangell and Petersburg. More of this cooperation is recommended.

10. *Housing.*—In view of the deplorable status of housing and the very evident deleterious effects on health, immediate steps should be taken to remedy this situation. Because of the excessive costs of construction it is essential that the federal government take cognizance of and direct action to supply adequate funds for the solution of the problem.

11. *Arctic Institute.*—An Arctic Institute for the study of the Arctic and its bearing on health, sanitation, nutrition, engineering construction, food, clothing and footwear is recommended. This should be set up at the University of Alaska with federal funds, and it should coordinate the efforts of the armed forces and the various federal agencies. The resultant effects on the civilian economy of efficient means of heating, construction, sewage and water supply would be a boon to Alaskan development and defense.

# Clinical Notes, Suggestions and New Instruments

## LEUKOPENIA FOLLOWING THE USE OF PROPYLTHIOURACIL

WILLIAM J. EISENMENGER, M.D.
and
J. MURRAY STEELE, M.D.
New York

Propylthiouracil is generally conceded to be the least toxic antithyrotoxic agent at the moment. Serious reactions to this drug are almost lacking in the literature. Reports of two febrile and urticarial reactions in 129 cases[1] and of 1 case of leukopenia and sore throat in a series of 110 cases[2] have appeared. Astwood and VanderLaan have now treated over 100 patients without the development of any significant side effect.[3] In 260 patients treated with the drug at the Lahey Clinic depression of the white blood cell count has been noticed in 5 instances.[4] The development of pronounced leukopenia in a patient under treatment with this drug was therefore considered of sufficient importance to report.

A second point of interest in the case is the increasing degree of thyrotoxicosis that developed while propylthiouracil was being administered in what was thought to be an adequate maintenance dose.

### REPORT OF CASE

A woman aged 65, a housewife, was admitted to this hospital on Feb. 3, 1946 with a chief complaint of weakness of four years' duration, which had become so extreme in the six weeks prior to admission that she was not able to walk or stand unsupported. She had also progressively lost 56 pounds (25 Kg.) in weight (170 to 114 pounds) during the previous year. For a period of six months she had noted excessive diaphoresis and a thinning of the texture of her hair. She had not been nervous or irritable, nor had she suffered palpitation or gastrointestinal symptoms.

Physical examination revealed a short, elderly woman with evidence of considerable recent loss of weight. Tremor and diaphoresis were absent. The common eye signs of thyrotoxicosis were lacking. There was a fulness in the suprasternal notch and a shift of the larynx and trachea to the left. A large mass of thyroid gland at the base of the neck on the right side extended downward into the superior mediastinum. A hard nodule 2 cm. in diameter was felt in the midst of this mass. The heart was moderately enlarged, the apical impulse being in the sixth left intercostal space, just outside the midclavicular line. The blood pressure was 170 systolic and 60 diastolic in mm. of mercury, and the pulse rate was 80. Normal sinus rhythm was present. Roentgen examination confirmed the impression of substernal extension of an enlarged thyroid gland. The basal metabolic rate was plus 54 per cent. The blood serum cholesterol determination was 173 mg. per hundred cubic centimeters. The hemoglobin level and the red blood cell count were normal, and the leukocytes ranged around 7,000 per cubic millimeter, with 65 per cent polymorphonuclear cells.

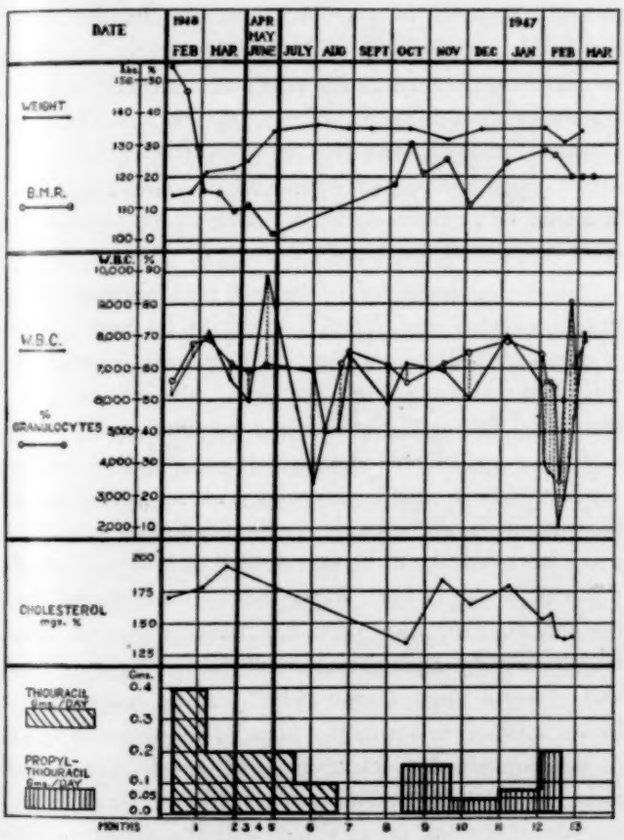
Because surgical removal of the thyroid appeared difficult, a trial of chemotherapy was decided on. Thiouracil, 0.1 Gm. four times a day, was administered, and the dose was reduced after one month to 0.1 Gm. twice a day, because the basal rate of the patient had fallen to nearly normal levels. In the

From the New York University Division, Lenox Hill Hospital.

1. McGavack, T. H.; Gerl, A. J.; Vogel, M., and Schutzer, S.: Clinical Comparison of the Effectiveness of 6-N-Propylthiouracil and 2-Thiouracil as Antithyrotoxic Agents, Am. J. Med. **2**: 144, 1947. Reveno, W. S.: Propylthiouracil in Thyrotoxicosis: Observations on Fifty-Four Patients, J. A. M. A. **133**: 1190 (April 19) 1947.
2. McCullagh, E. P.; Ryan, E. J., and Schneider, R.: Propylthiouracil in the Treatment of Hyperthyroidism, Cleveland Clin. Quart. **13**: 232, 1946.
3. Astwood, E. B., and VanderLaan, W. P.: Treatment of Hyperthyroidism with Propylthiouracil, Ann. Int. Med. **25**: 813, 1946.
4. Lahey, F. H., and Bartels, E. C.: Use of Thiobarbital and Propyl Thiouracil in Patients with Hyperthyroidism, Ann. Surg. **125**: 572, 1947.

outpatient department this dosage was continued for four months and then further reduced to 0.1 Gm. a day for one month. At this point, because the white blood cell count was low (3,400) and a differential count showed only 40 per cent polymorphonuclear cells, the administration of thiouracil was discontinued. There was a prompt return of the blood count to normal levels, as shown in the accompanying chart.

During this six month period of thiouracil therapy the patient had been doing well, as shown by her gain in weight and the return to normal of basal metabolic rates. However, within two months of the cessation of thiouracil therapy (October 1946) her basal metabolic rate rose to plus 30 per cent, the serum cholesterol level fell to 126 mg. per hundred cubic centimeters and, most important, she experienced her first episode of auricular fibrillation. Slight dyspnea occurred with this attack, but signs of congestive cardiac failure did not develop. The leukocyte and differential counts were normal at this time.




Laboratory Data

Because of the development of leukopenia on thiouracil she was put on a regimen of propylthiouracil, 50 mg. three times a day. During the next month another episode of auricular fibrillation occurred. As her serum cholesterol reading rose from 126 to 186 mg. per hundred cubic centimeters and her basal metabolic rate decreased, the dosage was reduced from 150 to 50 mg. a day. She remained on this regimen for six weeks until, in January 1947, a rising metabolic rate prompted an increase in the dosage to 75 mg. a day. After one month on this dosage she began to complain of exertional dyspnea and frequent episodes of irregular rhythm of the heart. Electrocardiograms showed that auricular fibrillation was present. The patient was hospitalized again, and normal sinus rhythm returned. The serum cholesterol determination had dropped to 150 mg. per hundred cubic centimeters, and the basal metabolic rate had risen to plus 29 per cent. Leukocyte counts remained at normal levels (6,000) with a normal differential count (65 per cent polymorphonuclear leukocytes).

The patient apparently exhibited signs of progressive thyrotoxicosis while receiving moderate doses of propylthiouracil for over three months. The dosage was increased to 50 mg. four times a day on Feb. 2, 1947, but symptomatic improvement did not occur. In fact, the serum cholesterol reading dropped further (to 135 mg. per hundred cubic centimeters), and the patient continued to lose weight. The white blood count fell steadily to 2,100 cells per cubic millimeter, associated with a sharp drop in polymorphonuclear cells to 22 per cent of the total count.

In view of the failure of the propylthiouracil to maintain the patient in adequate control on the usual dose, but more especially because of the danger of a continued fall in the number of granulocytes, administration of the drug was discontinued and surgical removal of the gland was recommended. On discontinuance of propylthiouracil the leukocytes rose quickly to a level of 8,000, the main rise taking place in the number of granulocytes, which rose rapidly from 22 to 82 per cent of the total leukocyte count.

The patient was prepared for surgical intervention by being given strong solution of iodine U. S. P. 10 drops three times a day for two weeks, without significant change in her basal metabolic rate and serum cholesterol level. Quinidine sulfate, 0.2 Gm. three times a day, was also given in an effort to prevent auricular fibrillation. A massive right lobe of the thyroid gland was then removed, and the relatively small left lobe was left. The operative procedure and the immediate postoperative course were uneventful except for several short bouts of auricular fibrillation.

### SUMMARY AND CONCLUSION

A case of thyrotoxicosis due to a large nodular goiter treated with thiouracil for six months and propylthiouracil for four months is reported because of reactions which appeared on use of these drugs.

1. Mild leukopenia developed after six months on thiouracil therapy.

2. Severe leukopenia developed after four months of treatment with propylthiouracil. Seventy-five milligrams of the drug a day proved insufficient to control the basal metabolic rate. During a short period of administration of 200 mg. of the drug a day in an unsuccessful effort to control the disease, leukopenia developed.

# Council on Foods and Nutrition

## ACCEPTED JUICES

*In order to encourage the production of fruit juices containing high natural levels of vitamin C, the Council on Foods and Nutrition accepts orange juice in which at least 40 mg. of ascorbic acid per hundred cubic centimeters of juice is conserved.*

*Attention is called to the fact that the products listed in this issue are not heat treated and should be consumed promptly after removal from refrigeration.*

*The following products meet the standards and rules established by the Council for fruit juices.*

JAMES R. WILSON, M.D., *Secretary.*

**The Vacuum Foods Corporation, Plymouth, Fla.**

MINUTE MAID BRAND QUICK-FROZEN CONCENTRATED ORANGE JUICE (27 fluidounces, 799 cc.).

SNOW CROP BRAND QUICK-FROZEN CONCENTRATED ORANGE JUICE (5⅓ fluidounces, 159 cc.).

These products, identical in composition, are distributed in containers of two sizes, namely, 27 fluidounces for institutions and 5⅓ fluidounces for individual use.

*Analysis* (submitted by manufacturer).—The analysis of the concentrate and of the product as reconstituted by the addition of three parts of water is as follows:

| | Concentrate | 1 + 3 Dilution |
|---|---|---|
| Total solids, % | 38.52 | 10.810 |
| Moisture (by difference), % | 61.48 | 89.190 |
| Protein (N × 6.25), % | 1.75 | 0.490 |
| Fat (ether extract), % | 0.09 | 0.030 |
| Crude fiber, % | 0.07 | 0.020 |
| Carbohydrates, % | 35.03 | 9.830 |
| Ash, % | 1.56 | 0.440 |
| Calories, per gram | 1.52 | 0.426 |
| Ascorbic acid, mg. per 100 Gm. | 159.30 | 44.700 |

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

535 North Dearborn Street - - Chicago 10, Ill.

Cable Address - - - - "Medic, Chicago"

Subscription price - - - - - Eight dollars per annum in advance

*Please send in promptly notice of change of address, giving both old and new; always state whether the change is temporary or permanent. Such notice should mention all journals received from this office. Important information regarding contributions will be found on second advertising page following reading matter.*

SATURDAY, OCTOBER 25, 1947

## THE EFFECTS OF MINERAL OIL

The use of mineral oil in foods such as imitation mayonnaise or salad dressing increased during the war because of the shortage of biologic fats and oils.[1] Such food substitutes are used extensively also in weight-reducing diets. Previous reports concerning the interference of mineral oil with the absorption of fat-soluble vitamins, particularly vitamin A and its precursor, carotene, were based mostly on animal experiments in which large quantities of mineral oil were used, compared with what would ordinarily be taken by man. Curtis [2] and his associates showed that the ingestion of mineral oil by human beings will prevent a rise in blood carotene consequent to simultaneous intake of foods rich in carotene; the subjects in this experiment were observed for only fifteen days. Recently Alexander [1] and his associates made similar observations on human beings for three to eight weeks. Group 1 did not take mineral oil. Group 2 took 1 tablespoonful of a product containing 83 per cent mineral oil and 2 per cent fat with the noon and evening meal daily. Group 3 took 1½ teaspoonfuls of the same product with noon and evening meals daily. Group 4 took 1 tablespoonful of mineral oil with noon and evening meals. Group 5 comprised 9 patients with psoriasis vulgaris, of whom 6 took 1 tablespoonful of mineral oil with noon and evening meals and 3 took 1 tablespoonful with each of the three meals. The diets of all subjects were unrestricted. The plasma carotene and vitamin A concentrations were determined by Kimble's method at frequent intervals. The results indicated that concomitant with the prolonged daily ingestion of mineral oil, either as such or in the form of mayonnaise dressing at meal time, the plasma carotene concentration decreased about 50 per cent. The decline was about the same for those using 2 tablespoonfuls as for those using 3 teaspoonfuls, and differences were not observed between those using regular mineral oil and those using the product previously mentioned. The decrease in plasma carotene was noted within one to two weeks; it progressed further in many cases as the intake of mineral oil continued. Neither significant changes in the plasma vitamin A nor untoward clinical manifestations occurred. Since it is well known that the concentration of vitamin A in the blood remains relatively constant for as long as six months in normal persons subjected to restricted intake of vitamin A and carotene, a conclusion could not be drawn on these subjects with regard to the effect of mineral oil on the supply of vitamin A as such to the body. The conclusion, however, was that in man the simultaneous ingestion of mineral oil with food prevents substantial amounts of food carotene, a precursor of vitamin A, from entering the body.

While many physicians believe that mineral oil is not absorbable and therefore can do no harm, some of it prescribed for constipation does pass through the intestinal wall and on into the liver. Alvarez [3] reviewed the work of Frazer, Stewart and Schulman, who found that if mineral oil was ingested without previous emulsification only a small percentage of it was absorbed but that when given in the form of a fine emulsion, as many persons take it, about one half of it went through the wall of the bowel. These workers found also that the fine emulsification necessary for this process could be effected by a combination of bile salts, oleic acid and glyceryl monostearate which can be found in the bowel. When taken in the form of the clear oil much of it is emulsified in the stomach or bowel. Frazer and associates demonstrated such absorption through the intestinal mucosa of rats histologically, biochemically and by actually counting the tiny oil droplets found in the blood, which could be easily seen in the cells of the intestinal wall. With a special chemical technic they found that from 35 to 60 per cent of the amount of emulsified oil was absorbed, an amount comparing favorably with the percentage of olive oil absorbed in control experiments. Stryker found in various experimental animals that the extent to which lesions appeared in the liver and lymph nodes was related to the time the animals had been given mineral oil. Rabbits fed mineral oil more than seven months showed numerous tiny white nodules in their intestinal wall, and vacuolization appeared in the mesenteric lymph nodes and liver. Similar changes were found in the tissues of men and women who were known to have used paraffin

1. Alexander, B.; Lorenzen, E.; Hoffmann, R., and Garfinkel, A.: The Effect of Ingested Mineral Oil on Plasma Carotene and Vitamin A., Proc. Soc. Exper. Biol. & Med. **65**:275 (June) 1947.

2. Curtis, A. C., and Kline, E. M.: Influence of Liquid Petrolatum on the Blood Content of Carotene in Human Beings, Arch. Int. Med., **63**: 54 (Jan.) 1939. Curtis, A. C., and Ballmer, R. S.: Prevention of Carotene Absorption by Liquid Petrolatum, J. A. M. A. **113**: 1785 (Nov. 11) 1939.

3. Alvarez, W. C.: The Absorption of Hydrocarbon Oil in the Small Intestine, Gastroenterology **9**: 315-317 (Sept.) 1947.

oil; in fact in 15 of 25 consecutive necropsies the lymph nodes revealed the presence of such droplets of oil.

These observations raise the grave question, Alvarez says, whether mineral oil can be used safely, year in and year out, as some persons use it; they also raise the question whether purveyors of food should ever be allowed to substitute mineral oil for the edible fats. The Council on Foods and Nutrition of the American Medical Association concluded in a report [4] published in 1943 that the indiscriminate use of mineral oil in foods and cooking is not in the interest of good nutrition and that any such use should be under careful supervision of a physician.

---

## THE PROBLEM OF CEREBRAL PALSY

The Joint Legislative Committee appointed by the legislature of the state of New York [1] to study cerebral palsy has made a preliminary report indicating that less assistance has been given to those with cerebral palsy than to the blind, the deaf and the crippled. At least 10,000 persons have this disability in New York.

Older writers considered birth trauma including cerebral hemorrhage, asphyxia or circulatory interference the most important causative factor of cerebral palsy. Recent investigations, however, support the original statement of Little that "the condition may present itself as a congenital affliction or as a result of diseases during infancy. Cerebral palsy is probably in most cases the result of variations in the structure of the brain." The abnormality may vary from the slightest physical handicap to subnormal mentality and severe physical disability with inability to meet the simplest personal needs. The misconception that the mental development of the patient with cerebral palsy is necessarily retarded needs correction. As a matter of fact, mentality is normal in most instances; whatever mental retardation is present is due to a lesion of the area of the brain concerned with the development of intelligence. This occurs in a limited percentage of patients.

Diagnoses of mental deficiency are made frequently because of the patient's appearance and poor score on psychometric testing, although accuracy in such tests depends on proper coordination, normal speech and good vision and hearing. The report points out that the evaluation of the extent of physical and mental retardation is difficult even when the diagnosis of the condition is almost self evident. Evaluation requires determination of the type of qualitative motor defect, the degree of handicap, the parts of the body involved, the amount of involvement, the developmental progress that has been made, the presence of associated or independent defects and the social situation of the patient and the patient's family.

Proper diagnosis of cerebral palsy depends on the training of more medical specialists supplemented by psychologic examiners and specially devised testing and diagnostic procedures which are capable of reaching the real person through the mask of physical handicaps which stand between him and the examiner.

Treatment cannot eradicate the original lesion. Specific treatment can be given for some of the defects, but the patient must be trained rather than treated. Whatever latent resources he possesses can be activated to the fullest extent. Training consists primarily of physical and occupational therapy to help the patient achieve better coordination of movements, to control hyperactive movements and to overcome involuntary movements through relaxation and similar functions.

Specialists estimate that 65 to 70 per cent of patients with cerebral palsy have normal mentality. Improvement in such patients extends from simply acquiring the capacity to dress and feed themselves to complete vocational rehabilitation.

Children and adults with cerebral palsy are entitled to the same educational services under the laws of the state of New York as are provided for other physically handicapped persons. The State Department of Education is authorized to provide vocational education and training, maintenance, textbooks and supplies and orthopedic appliances to the physically handicapped in order to prepare them for useful employment. However, the report stresses that the total of specialized treatment now available is small in proportion to the need. For most of those with cerebral palsy thorough and specialized diagnosis is not available. A survey by the Children's Bureau, then of the United States Department of Labor, published July 15, 1946, revealed that little progress has been made in the various states in meeting the needs of children with cerebral palsy. Medical, surgical and therapeutic services for such children are either absent or inadequate, both as to the number of children reached and the scope of services.

The report of the Legislative Committee emphasizes that the situation is rapidly improving. The programs in several states includes special institutions, appropriations for specialized centers in connection with state university medical schools and state subsidization of services from private institutions. States have met the problem in different ways. The report suggests the general objectives to be sought in attempting to develop a program for New York. Private interest in this problem is needed to supplement the work of the state in the care of so many other groups of the unfortunate.

4. Mineral Oil (Liquid Petrolatum) in Foods, Report of the Council on Foods, J. A. M. A. **123**: 967 (Dec. 11) 1943.

1. Preliminary Report of the New York State Joint Legislative Committee to Study the Problem of Cerebral Palsy, submitted to the legislature at the session of 1947, Legislative Document number 45.

# Current Comment

## MEDICAL CONDITIONS IN ALASKA

Elsewhere in this issue (p. 500) appears a special article on medical conditions in Alaska. This report was made by a group of physicians who were sent to Alaska by the Department of the Interior as representatives of the American Medical Association. The arrangements were made by a committee of the American Medical Association which is advisory to the Honorable J. A. Krug, Secretary of the Interior. Outstanding in this report is the fact that tuberculosis is the major health problem of Alaska, with a native death rate sixteen times the over-all death rate of the United States in 1944. The second great need of Alaska is sanitation, including improved water supplies and better sewage disposal. Third is the problem of venereal disease. With our present knowledge, it should be possible to control venereal disease in a community in a score of years. Finally, a shortage of beds prevails not only in the general hospitals of Alaska but also in sanatoriums for the tuberculous. The Commissioner of Health of Alaska, Dr. C. Earl Albrecht, has emphasized these needs. Another team developed from Southwestern Medical College in Dallas, Texas, and including six physicians recently gave similar help for some weeks to the Navajo people on the reservation that they occupy at Fort Defiance, Ariz. Visits will be made in the near future to Puerto Rico and the Virgin Islands by other teams of physicians now being assembled. The projects were approved by the House of Delegates of the American Medical Association, and the committee in charge is representative of the executive committee of the Board of Trustees and officers of the Association. Here is practical cooperation extending to the indigent wards of our government medical service which would not otherwise be available.

## THE WORLD MEDICAL ASSOCIATION

In the Organization Section in this issue of THE JOURNAL (p. 518) appears a preliminary report by Dr. Charles Hill, secretary of the British Medical Association, of the organization and first meeting of the World Medical Association in Paris, September 18. The representatives of the American Medical Association in this meeting were Dr. Elmer L. Henderson, chairman of the Board of Trustees, and Dr. L. H. Bauer, member of the Board of Trustees. As alternate delegates Dr. R. L. Sensenich, President-Elect of the Association, and Dr. Ernest E. Irons, Secretary of the Board of Trustees, also attended. Although world peace is a fundamental objective of the World Medical Association, the report indicates that the meeting was not wholly peaceful. Forty-eight nations were represented. The two principal objectives determined were promotion of closer ties among the national medical organizations and among the physicians of the world and study and report on professional problems that confront the members of the medical profession in various countries. Much consideration was given to the extent to which the professions of various countries would be represented with an ultimate agreement that each national medical association should have two votes but that membership would be available for any other national or territorial medical association representative of the medical profession in its country or of the medical profession of an ethnic group within the country. Apparently medical political attitudes prevailed at least for a while because the South American countries acted as a bloc during the early days of the session under the leadership of Dr. Hurtado of Cuba, who, strangely, was an official delegate from Costa Rica. In the course of the considerations the American delegation submitted a report on its efforts to secure funds for the functioning of the World Medical Association. It was agreed that the office of the secretary should be in North America, probably in New York city, since the headquarters of the United Nations and the World Health Organization will also be in New York. Among the significant actions taken was a resolution that German delegates would not be admitted to the World Medical Association until organized medicine in Germany condemned past criminal acts of German physicians.

## THE MOBILITY OF BONE

The introduction of the use of stable isotopes in experimental biology soon resulted in the demonstration that protein of the body exists in equilibrium with the tissue amino acids and that it is constantly being broken down and resynthesized. That this kind of equilibrium exists also between the apparently inert bones and inorganic ions is shown by accumulating evidence. In 1945 it was reported [1] that precipitates which are formed from solutions of the approximate inorganic composition of blood have a composition similar to the inorganic portion of bone and that the solubility of these precipitates corresponds closely to the amount of calcium and phosphate present in the plasma. The exact composition of these inorganic precipitates varies with the composition of the supernatant solutions, in much the same way that the composition of bone varies with the inorganic composition of the plasma.[2] The experimental use of radioactive phosphorus resulted in demonstration that the phosphate of bone is rapidly exchanged in the living animal with the phosphate of serum; this exchange with whole bone occurs almost as rapidly as the exchange between powdered bone and the surrounding solution.[3] Since the reaction appears to occur on the crystal surfaces of the bone, some mechanism apparently facilitates diffusion of the phosphate through the bone. These experiments show the exchange relations which exist between the bone and the tissue fluids and also support the thesis that the diet influences the healing of fractures and the health of the bones.

1. Kuyper, A. C.: J. Biol. Chem. **159**: 411, 1945.
2. Sobel, A. E.; Rockenmacher, M., and Kramer, B.: J. Biol. Chem. **158**: 475, 1945.
3. Falkenheim, M.; Neuman, W., and Hodge, H. C.: J. Biol. Chem. **169**: 713, 1947.

# ORGANIZATION SECTION

## Official Notes

### CONFERENCE OF STATE MEDICAL ASSOCIATION SECRETARIES AND EDITORS

The annual conference of State Medical Association Secretaries and Editors will be held in the American Medical Association Building, Chicago, Nov. 7 and 8, 1947.

PROGRAM

FRIDAY MORNING, NOVEMBER 7

Assembly Hall—Ninth Floor

10:00 a. m. *Call to Order.* E. L. HENDERSON, Chairman of the Board of Trustees of the American Medical Association.
*Election of Chairman*

10:20 a. m. *Technics in Preparing and Displaying Exhibits for Lay Groups.* BRUNO GEBHARD, Director of the Cleveland Health Museum.

10:40 a. m. *Effective Scientific Programs.* OSCAR B. HUNTER, Washington, D. C.

11:00 a. m. *Survey of Group Practice.* G. HALSEY HUNT, U. S. Public Health Service.

11:20 a. m. *The Private Physician in the School Health Program.* CHARLES H. KEENE, Editor of the *Journal of School Health.*

11:40 a. m. *General Discussion*

12:00 m. *Luncheon*

*PANEL DISCUSSION ON THE PROGRESS OF PREPAYMENT MEDICAL CARE PLANS*

2:00 p. m. *Medical Society Plans.* JAMES R. MCVAY, Chairman of the Council on Medical Service of the American Medical Association.

2:15 p. m. *Cooperatives.* Mr. CHARLES H. CROWNHART, Secretary of the State Medical Society of Wisconsin.

2:30 p. m. *Associated Medical Care Plans, Inc.* L. HOWARD SCHRIVER, President of Associated Medical Care Plans, Inc.

2:45 p. m. *Private Insurance Plans.* ALFRED W. ADSON, Member of the Council on Medical Service of the American Medical Association.

3:00 p. m. *General Discussion*

FRIDAY AFTERNOON, 3:30

*ROUND TABLE DISCUSSIONS*

PUBLIC RELATIONS

Room 5—Fourth Floor

Moderator: L. FERNALD FOSTER, Secretary of the Michigan State Medical Society.

Leaders of Discussion: HAROLD M. CAMP, Secretary of the Illinois State Medical Society.
Mr. HARVEY T. SETHMAN, Executive Secretary of the Colorado State Medical Society.

RELATIONS WITH LABOR

Lunch Room—Fifth Floor

Moderator: NORMAN M. SCOTT, Director of Medical Care Plans, Medical Society of New Jersey.

Leaders of Discussion: WALTER E. VEST, Editor of the *West Virginia Medical Journal.*
B. B. SOUSTER, Secretary of the Minnesota State Medical Association.

FEDERAL AND STATE LEGISLATION

Lunch Room—Fifth Floor

Moderator: W. P. ANDERTON, Secretary of the Medical Society of the State of New York.

Leaders of Discussion: P. E. BLACKERBY, Secretary of the Kentucky State Medical Association.
Mr. THOMAS R. O'BRIEN, Executive Secretary of the Missouri State Medical Association.

RURAL MEDICINE

Room 6A—Fourth Floor

Moderator: R. B. ADAMS, Secretary of the Nebraska State Medical Association.

Leaders of Discussion: H. T. CARAWAY, Secretary of the Medical Association of Montana.
HOLMAN TAYLOR, Secretary of the State Medical Association of Texas.

PLANNING AND CONDUCTING STATE MEDICAL CONVENTIONS

Assembly Hall—Ninth Floor

Moderator: JOHN C. PARSONS, Secretary of the Iowa State Medical Society.

Leaders of Discussion: W. M. HARDY, Secretary of the Tennessee State Medical Association.
Mr. JOHN HUNTON, Executive Secretary of the California Medical Association.

Assembly Hall—Ninth Floor

4:45 p. m. *Report on Cooperative Medical Advertising Bureau.* MR. ALFRED J. JACKSON, Director of the Cooperative Medical Advertising Bureau.

FRIDAY EVENING

Palmer House

6:30 p. m. *Dinner for Secretaries*

8:00 p. m. *Secretaries' Forum: How Can the Activities of the American Medical Association and State Medical Societies Be Better Coordinated?*

Moderator: JULIAN P. PRICE, Secretary of the South Carolina Medical Association.

Speakers: CREIGHTON BARKER, Secretary of the Connecticut State Medical Society.
P. T. TALBOT, Secretary of the Louisiana State Medical Society.
Mr. CHARLES S. NELSON, Executive Secretary of the Ohio State Medical Association.
FRANK J. MILLOY, Secretary of the Arizona State Medical Association.

9:00 p. m. *General Discussion* led by GEORGE F. LULL.

6:30 p. m. *Dinner for Editors*

8:00 p. m. *State Medical Journal Clinic*
(*California Medicine*, the *Connecticut State Medical Journal*, the *Ohio State Medical Journal* and the *Wisconsin Medical Journal* have been studied, with permission of the respective editors, by the speakers with a view of offering constructive suggestions.)

Moderator: Mr. THEODORE WIPRUD, Secretary of the Medical Society of the District of Columbia.

Speakers: Format and Topography. Mr. ROBERT H. ROY, Chief Engineer, Waverly Press, and Associate Professor of Industrial Engineering at Johns Hopkins University.
Literary Aspects. Mr. HARRY SHAW, General Editor, Harper and Brothers.
Editorials. Mr. JOHN STORM, Executive Editor of *Hospitals.*
Scientific Material. MORRIS FISHBEIN, Editor of THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION.

9:00 p. m. *Question Period*

SATURDAY MORNING, NOVEMBER 8

Assembly Hall—Ninth Floor

10:00 a. m. *Reports of Round Table Discussions*
Each Round Table Discussion will be summarized so that members of the Conference who could not attend some of the Round Tables will be sufficiently informed to participate in the general discussion which will follow reading of the reports.

11:30 a. m. *World Medical Association.* LOUIS H. BAUER, Member of the Board of Trustees of the American Medical Association.

12:00 m. *Election of Program Committee for 1948 Conference*

# World Medical Association

NOTE: Following is a report by Dr. Charles Hill, secretary of the British Medical Association, of the first meeting of the World Medical Association in Paris, September 18. Dr. Hill is honorary secretary of the World Medical Association pending the establishment of a permanent office and the appointment of a full time secretary. Dr. J. A. Bustamante of Havana, Cuba, secretary of the Pan-American Medical Confederation, was appointed as honorary assistant secretary for matters pertaining to the Latin American countries.—ED.

### CONSTITUTION

During the first part of the meeting, which took the form of a conference of representatives of national medical associations, various amendments were made in the draft articles and by-laws, which will now be revised in accordance with the decisions of the conference and issued with the minutes. When the constitution, thus amended, was adopted by the conference, it was formally declared that:

In the city of Paris at 3:40 p.m., on September 18, 1947, the World Medical Association came into being.

The meeting then became the first annual meeting of the general assembly, and Professor Eugène Marquis (France) was installed as the first president of the association.

Dr. Charles Hill (Great Britain) was appointed acting honorary secretary of the meeting.

### HEADQUARTERS

It was decided that the offices of the Association should be situated in North America, the exact location being left for decision by the council. One of the main factors influencing this decision was the desirability of close and constant contact with the United Nations and World Health organizations (U. N. O. and W. H. O.) which have their headquarters in New York.

### OFFER OF FUNDS FROM THE UNITED STATES

The delegates from the United States reported that certain industrial "friends of the American Medical Association," being convinced of the potential value of the World Medical Association to medicine and to the promotion of world peace and being desirous of helping to establish it on a sound financial basis, had offered to guarantee an income of $50,000 for the first year and, if necessary, to continue a similar contribution for a further four years. The money was intended to be used for the provision of a permanent office, the remuneration of a full time secretary and staff and the running costs of the secretariat. An American committee of physicians and laymen had been set up to administer the funds. The American delegates emphasized that there was no intention of determining or interfering with the policy of the World Medical Association, the committee's only duty being to approve the general purpose of the projects for which the Association desired to use the donors' money. After a prolonged discussion the association decided by a majority vote to accept the generous offer of its American friends and adopted the following resolutions:

*Resolved*, That the general assembly accept with gratitude the offer of the friends of the American Medical Association and place on record its deep appreciation of their generosity in making available funds sufficient for the establishment of the World Medical Association on a satisfactory basis.

That the funds thus made available be utilized to defray expenditure under the following headings: (*a*) the remuneration and expenses of the secretary, other officials and clerical staff; (*b*) the rent, rates and other disbursements in connection with the official headquarters; (*c*) the general office expenses of the headquarters office staff; (*d*) the cost of the publication of the association's official bulletin or journal, and (*e*) the travelling costs of the council.

That the cost of the developments previously listed be estimated at not more than $50,000 for the first year.

That the Council be authorized to act on the assembly's behalf in appointing the secretary of the World Medical Association and to make all other staffing arrangements, regional and other.

That the Council be instructed to explore the possibility of making arrangements for gift funds to the World Medical Association to be made tax-free.

That member associations be recommended to consider the formation of World Medical Association supporting committees in their several countries.

That the council be authorized to prepare plans of development, to enter into any necessary consultations and to submit its proposals to the general assembly.

That nothing in these resolutions shall diminish the authority of the general assembly for the full control of the policy and affairs of the Association as provided in article 8.

### SUBSCRIPTION

The acceptance of the American offer does not, of course, relieve the association of the necessity of collecting its own subscription income. After consideration of the report of the honorary treasurer and of the possible methods of assessing subscriptions, the general assembly adopted the following resolutions:

*Resolved*, That the subscription of each member association be calculated at a flat rate per member with a minimum total and a maximum total, and that the flat rate per member be 20 Swiss centimes, with a minimum of 1,000 Swiss francs and a maximum of 10,000 Swiss francs.

### MEMBERSHIP ROLL

In accordance with article 5 (I) those national medical associations which were represented at the London conference in September 1946 were accepted as founder members. During 1946-1947 the Organizing Committee, which was instructed by the conference to proceed with the organization of the association, invited all national medical associations to apply for membership, and those applicants which appeared to fulfil the conditions of article 5 (II) were accepted as members.

As soon as the constitution was adopted at the Paris meeting, the procedure laid down in by-law 1 came into operation. Italy (La Federazione Nazionale degli Ordini dei Medici Italiani) made a written application for membership to the general assembly and was accepted. Certain difficulties then arose in connection with the associations in Latin America, and the general assembly eventually decided to request the council to submit for examination by next year's general assembly the applications of all member associations.

### SECRETARIAT

As has already been stated, the general assembly left to the council the problem of the general organization of the secretariat. However, it considered the desire expressed by the Latin American associations for the specific recognition of the Spanish culture in the association's organization. They proposed the adoption of Spanish as a third official language and the appointment of a Spanish assistant secretary, whom they offered to finance without cost to the association. The assembly adopted the first proposal. With regard to the second, it recognized that with the development of the association's work it might become desirable to appoint perhaps several assistant secretaries in different parts of the world. It therefore instructed the council to include this matter in its consideration of the general organization of the secretariat and recommended for acceptance the kind offer of the Latin American associations.

### PROXY VOTING IN ASSEMBLY

The general assembly referred to the council for consideration a suggestion by Australia that provision should be made in the by-laws for voting by proxy in the general assembly in order that far distant member associations which might be unable to send delegates to a meeting of the general assembly would not thereby lose their voting power.

### WAR CRIMES

After a discussion of the motions on the agenda by Denmark and Great Britain and the British memorandum relating to the attitude of the members of the medical profession toward war crimes, and after hearing statements by members of the assembly and by a French medical victim of war crimes, the assembly appointed a small committee to formulate a recommendation. The following report of the committee was subsequently adopted by the assembly:

*Resolved*, That a report on crimes committed since 1933 by physicians and medical organizations in Germany and other countries and on this violation of the medical ethic be prepared and made available to physicians throughout the world.

That the World Medical Association solemnly condemns the crimes against human beings committed by certain members of the medical profession such as are described in the British memorandum.

That every doctor, at the time of receiving his medical degree or diploma, be required to subscribe to the following oath:

> "My first duty, above all other duties, written or unwritten, shall be to care to the best of my ability for any person who is entrusted or entrusts himself to me, to respect his moral liberty, to resist any ill treatment that may be inflicted on him and, in this connection, to refuse my consent to any authority that requires me to ill treat him.
>
> Whether my patient be my friend or my enemy, even in time of war or in internal disturbances, and whatever may be his opinions, his race, his party, his social class, his country or his religion, my treatment and my respect for his human dignity will be unaffected by such factors."

That the World Medical Association endorse judicial action by which members of the medical profession who shared in war crimes are punished.

That the World Medical Association request the German medical syndicates to make the following public declaration:

> A. We, members of the German medical syndicate, are aware of the very large number of acts of cruelty committed, both by individuals and collectively, since 1933 in mental hospitals and in concentration camps and of the violation of the medical ethic. These acts have resulted in the death of some millions of persons. A large number of our members have been implicated in these acts, either as instigators or as technical agents or as actual perpetrators.
>
> B. We regret that the organized medical profession in Germany has not made any protest and has been content to ignore these acts, of which it could not have been unaware.
>
> C. We undertake solemnly to condemn these crimes, to expel from our organization the criminals who have committed them and to remind all our members of the respect due not only to life but to human personality, dignity and liberty.

The assembly instructed the council to prepare a report incorporating these resolutions and also to take into consideration the following motion by the Netherlands: "That the council be instructed to prepare a report on the collaboration of medical practitioners in the preparation of means of warfare."

### MATTERS REFERRED TO COUNCIL

During the course of the meeting the general assembly also referred the following matters to the council for appropriate action or investigation and report:

1. The general arrangements for the organization and publication of a bulletin or journal.
2. The preparation of a report on the inquiry into the present position of the medical profession in relation to the state.
3. The motions of Luxembourg, supported by Australia, recommending the preparation (*a*) of a comparative statement on standards of training for the medical profession and conditions of registration and (*b*) of a comparative statement on the qualifications of specialists.
4. The following motions by India: (*a*) "That the council be requested to study and report on the question of the advertisement of cures and medicines in the lay press" and (*b*) "That the council be requested to study and report on the question of unqualified and unauthorized medical practice."
5. The preparation of standing orders to govern the procedure of meetings of the general assembly.
6. The appointment of auditors.

### SECOND ANNUAL MEETING OF GENERAL ASSEMBLY 1948

The general assembly decided to hold its 1948 meeting in Prague, Czechoslovakia, the exact date being left to the council to decide.

### PRESIDENT-ELECT, 1947-1948

The general assembly elected Dr. J. Stucklich (Czechoslovakia) to preside over its annual meeting in 1948. He therefore becomes president-elect for the year 1947-1948.

### TREASURER, 1947-1950

The general assembly elected Dr. O. Leuch (Switzerland) as treasurer of the Association for the period of 1947-1950.

### COUNCIL, 1947-1948

The general assembly elected the first council. Dr. Zahor (Czechoslovakia) and Dr. Glorieux (Belgium) having resigned after election, the council for 1947-1948 is composed as follows: president ex officio, Professor E. Marquis, France; president-elect, Dr. J. Stucklich, Czechoslovakia; treasurer, Dr. O. Leuch, Switzerland; chairman, Dr. T. C. Routley, Canada, and vice chairman, Dr. D. Knutson, Sweden. Other members of the council are Drs. L. H. Bauer, United States; J. A. Bustamante, Cuba; P. Cibrie, France; A. Hartwich, Austria; P. Z. King, China; J. A. Pridham, Great Britain; S. C. Sen, India, and L. G. Tornel, Spain.

At the conclusion of the general assembly's proceedings the council held its first meeting.

Pending the establishment of a permanent office and the appointment of a full time secretary, the council appointed Dr. Charles Hill (Great Britain) as honorary secretary of the association with temporary headquarters at B. M. A. House, London.

---

## Washington Letter

*(From a Special Correspondent)*

Oct. 23, 1947.

### Funds for New Army Medical Library

Brig. Gen. George E. Armstrong, acting surgeon general of the Army, told the fourth annual meeting of the honorary consultants to the Army Medical Library that the War Department would again request funds from Congress next year for a new building. Cost is estimated around $16,000,000, four times the amount sought nine years ago. Congress will have to amend existing enabling legislation before an appropriation can be requested. Col. Joseph H. McNinch, library director, reported that the present building at Seventh Street and Independence Avenue, S.W., is inadequate. He said that one of the library's greatest needs is a permanent director. At present, Army officers are appointed to the post every four years. General Armstrong explained that the War Department already is planning to acquire a career director. Among other speakers were: Gen. Paul R. Hawley, medical director of the Veterans Administration; Walton B. McDaniel, librarian, Philadelphia College of Physicians, and Chauncey D. Leake, dean of the University of Texas School of Medicine. New officers elected were: president, Dr. Leake; vice president, Wilburt C. Davison, Raleigh, N. C., dean of Duke University School of Medicine, and secretary-treasurer, reelected, Col. Harold W. Jones, M. C., U. S. Army, retired. Dr. Reginald Fitz, Boston, medical history lecturer, Harvard University, was appointed to the executive committee.

### Health Service Announces Cancer Research Grants of $363,749

The U. S. Public Health Service has announced that grants totaling $363,749 have been made to nearly a score of colleges and other institutions for cancer research and control. They are part of the $14,000,000 campaign against cancer authorized by Congress for the fiscal year ending next June 30. The projects were recommended by Dr. A. V. Deibert of the National Cancer Institute and approved by the National Advisory Cancer Council. The grants include research for improved cancer instruction technics, a national survey of cancer clinics, evaluation of different cancer control and detection methods and fundamental studies of the growth, development and treatment of cell malignancies. A joint Public Health Service and District of Columbia survey revealed that Washington has the highest cancer incidence of twelve cities surveyed.

### Dr. Paul B. Magnuson Takes Number Two Spot in Veterans Administration

Dr. Paul B. Magnuson, Chicago surgeon who helped set up the Dean's Committee program which links Veterans Administration hospitals with the nation's best medical centers, has been appointed chief of professional services for the Veterans Administration Medical Department. This is the number two position. In the event that Dr. Hawley succeeds Gen. Omar Bradley as head of the agency when the latter is appointed Army Chief of Staff, Dr. Magnuson will be in line for the medical directorship. Dr. Magnuson succeeds the late Brig. Gen. Elliott C. Cutler, who died last August in Boston.

# JOINT COMMITTEE FOR THE COORDINATION OF MEDICAL ACTIVITIES

## Report of Meeting in Chicago, April 26

The Joint Committee for the Coordination of Medical Activities met Saturday, April 26, 1947, in the Board Room of the American Medical Association Building in Chicago. The Chairman, Dr. Ernest E. Irons, called the meeting to order at 10:10 a. m. Members and liaison members present were:

| | |
|---|---|
| Col. George E. Armstrong | Dr. George F. Lull |
| Dr. Walter L. Bierring | Dr. James M. Mason |
| Mr. Graham L. Davis | Dr. J. J. Moore |
| Dr. W. Palmer Dearing | Dr. H. B. Mulholland |
| Dr. Warren F. Draper | Dr. James E. Paullin |
| Capt. William E. Eaton | Lieut. Col. William N. Piper |
| Dr. Lester J. Evans | Rev. Alphonse M. Schwitalla, S.J. |
| Dr. Morris Fishbein | Dr. R. L. Sensenich |
| Dr. J. F. Hammond | Dr. H. H. Shoulders |
| Dr. E. L. Henderson | Mrs. M. V. Shuler |
| Mr. J. W. Holloway Jr. | Miss Mary Switzer |
| Dr. Ernest E. Irons | |

### HOSPITAL RESIDENCIES

The Chairman read the following statement received from Dr. Victor Johnson, a member of the Joint Committee, who was unable to be present:

Some time before the war ended the Council on Medical Education and Hospitals estimated that it would probably be necessary to double the number of residency positions to meet the needs of returning medical officers. This goal has now been achieved, since there are now 10,422 residency positions as compared with 5,256 in 1941. Even this expanded number is insufficient to meet the demands, because the Asiatic phase of the war ended much sooner than was expected and the rate of discharge of medical officers was much more rapid than had been estimated. In any case, expansion of residency opportunities beyond the present number could probably be effected only with a serious diminution in quality.

### LICENSURE STATISTICS FOR 1946

The following statement on licensure statistics, also received from Dr. Johnson, was read by the Chairman:

In February 1946 the Federation of State Medical Boards published a statement based on a canvass of respective licensing boards of the country on several points pertaining to the licensure of returning medical officers. The text of this report indicates that medical officers will be required to satisfy peacetime licensure regulations except in a few instances in which special consideration is given to such applications. However, in several ways the medical licensing boards have attempted to be of assistance to medical officers returning to the private practice of medicine; for example, the issuance of temporary permits, the relaxation of the one year internship requirement and the licensure of physicians by reciprocity and endorsement of credentials. At present there is only one state, Florida, which requires a written examination of all applicants for medical licensure. Reciprocity meetings have been held at more frequent intervals than previously. The advantage of this procedure is evidenced by the fact that in 1946 there were 9,567 so licensed as compared with 3,615 in 1945. There was an increase of 1,010 in the number registered after examination. The total number of physicians licensed in 1946 was 16,121, whereas in 1945 there were 9,159 licenses issued, an increase of 6,962.

Dr. Bierring said that the large number of physicians licensed by reciprocity in 1946 is an indication that a good deal of flexibility has developed in the requirements of state licensing boards, that while at first the boards were adhering to prewar standards considerable leniency has gradually been brought about, and that this has been accomplished as much by conference as by any kind of regulation or definite action. He said further that the only difficulty has been with graduates of unapproved medical schools who, by reason of their military service, believed they should be entitled to additional consideration; that there were instances of graduates of unapproved schools who had had three years or more of very creditable military service, but the average state board hesitated to consider such service as an additional qualification although there were a few instances in which exceptions were made.

Miss Switzer stated that at one time there were some three hundred graduates of unrecognized schools in the Army. In reply to a query from Miss Switzer, Dr. Bierring said that the state of Massachusetts now has a definite medical practice act which admits to examination only graduates of approved medical schools and now is gradually entering into reciprocity agreements with other states. He also said that Florida, to which many specialists go in the winter months, will not accept reciprocity and that he thought the situation in that state is mostly traditional and political.

Dr. Bierring informed the Committee that a committee, or society, has been organized in New York which has sent communications to the Federation of State Medical Boards and, he thought, to the state boards, appealing for "justice" for medical graduates of the extramural schools of Scotland and Ireland and of certain similar European schools, claiming that the National Board and the state boards have been very discriminatory against them. He said that there were about three hundred American students of these extramural schools—mostly men who had not qualified for admission to American schools—who were stranded in this country at the outbreak of the war in Europe in 1939 and unable to get back to their studies.

After further discussion and on motion of Father Schwitalla, it was decided that the Joint Committee for the Coordination of Medical Activities would request the Council on Medical Education and Hospitals to secure, if possible, a list and an authoritative statement as to the present status of the schools in Great Britain that are designated as extramural.

### REPORT OF SUBCOMMITTEE ON SPECIALTY BOARD FOR GENERAL PRACTITIONERS

In asking for a report from the Subcommittee on Specialty Board for General Practitioners, the Chairman stated that this is one of the most vital problems confronting American medicine today.

Dr. Sensenich, member of the Subcommittee, presented the following statement:

This matter goes much beyond the establishment of a specialty board. First, the specialty boards were set up to improve standards and to establish qualifications necessary for certification of physicians as specialists in various fields of medicine. Such a certified specialist presumably then was qualified for practice in a restricted field, which, also presumably, automatically took him out of competition with physicians practicing in other fields or in general medicine. On the other side is the general practitioner. It would seem necessary to establish some kind of educational machinery by which standards might be maintained for those who are not restricting their work to particular fields and are not diplomates of boards. That part is not new. Some years ago a survey was made by the Council on Medical Education and Hospitals of postgraduate education courses offered in the various states. While there was not any particular demand for such courses at that time, they were necessary if specialty boards were to be established. A number of states were not interested. Several had so-called postgraduate courses of which they were very proud and with which they did not wish any interference. In many instances the best courses were tied up with state universities, were limited, and no credit was given. They served a purpose, however, in that they gave opportunity for education and for public relations between the schools and the members of the medical profession.

Some provision must be made to give the general practitioner opportunity to keep his work up to a high standard. Also, there must be, at the least, a reevaluation of the educational machinery at the medical school and hospital level. The tendency away from rotating internships is undesirable. Many of the teaching hospitals offer no rotating internships. It is much to the advantage of the individual specialist to have an intern who is limited to the specialist's own service, and this attitude of the teaching staff goes on through the hospital.

The exclusion of patients from hospitals that are teaching hospitals is a matter of grave concern. The specialty teacher obviously needs facilities for the care of his particular group of patients; on the other hand, there would not seem to be much reason why the patient should not be admitted if his illness is not in a special category. From the teaching standpoint, there seems to be no reason why the patient of a general practitioner could not be admitted. Some hospitals are excluding patients of those who are not diplomates of the specialty boards.

Dr. Bierring spoke for the Subcommittee as follows:

Dr. Sensenich has presented an assemblage of the opinions the Subcommittee has gained by contact with many persons. He has emphasized first the fact that it is one of the most important problems with which the profession has to deal. There is no uniformity of opinion as to what constitutes general practice. It is not a specialty; it is the cornerstone of all practice.

When the American Board of Ophthalmology, the first of the specialty boards, was formed in 1916, it had a definite background. There were special societies in ophthalmology, special journals and special chairs in the schools, and it was therefore easy to formulate a Board and to determine standards that the specialists should meet in order to be so classified. The next boards developed more or less on that same basis; they had something from which to draw. There is no such basis in general practice. The American Medical Association at last has established a Section on the General Practice of Medicine, but otherwise the Association in its Scientific Assembly constitutes a program presented usually by specialists.

How can a basic foundation or background for this new classification be established? It is of fundamental importance. It goes back to undergraduate teachers, so many of whom are specialists and unconsciously bring their specialties into their teaching. The purpose of the present scheme of medical education is to train general practitioners, those who will be proficient in the diagnosis of general conditions. If this is to constitute the major part of the future practice of medicine, there should be special training and teachers in the schools who can satisfactorily present that phase.

It has been said that many of the teaching hospitals have found it practical to have internships devoted to special departments. The move that has been made by Cook County Hospital and other large hospitals to increase the rotating internship is a move in the right direction. There has been established at the University of Colorado a three year rotating residency in general practice. Much could be done by means of extension courses planned on a national basis.

I think that the Subcommittee considers this a problem that should be presented to the American Medical Association. The majority of the members of the Association are what is known as general practitioners. I cannot define a general practitioner, but I think every one has in mind what a general practitioner should do. It is assumed that the approved medical schools train just that sort of man—one who can go into any community and take care of 80 per cent of the practice and who can recognize special conditions. The National Board of Medical Examiners has a very comprehensive examination which, when passed successfully, entitles a man to recognition that he is a little better trained than the average medical graduate. The National Board does not recognize a man as a specialist just because he has had special training. It asks that he have had experience and association with men in his field. A plan for certification in general practice should include an examination or some form of qualification procedure after five years, or perhaps ten years of general practice, in which the Certificate of the National Board of Medical Examiners might be considered as a part of the qualification. It would be unwise to follow Indiana and formulate overnight a specialty board of general practice. Such a step should not be taken hastily. It would seem that the best way would be through the American Medical Association and through the formation of a committee which will study the situation and offer a possible solution to the problem.

### LEGISLATION IN CONGRESS

Mr. J. W. Holloway Jr., director of the American Medical Association's Bureau of Legal Medicine and Legislation, presented a statement on pending legislation in Congress, which, after discussion, was accepted.

### RURAL MEDICAL SERVICE

At the request of the Chairman, Dr. Mulholland gave the following résumé of activities of the Committee on Rural Medical Service:

The Committee on Rural Medical Service appointed its executive committee to meet with representatives of four farm organizations in Chicago in May. This was done at the request of the farm groups. The chairman of each state committee on rural health has been asked to present a report of his committee's activities, so that a full report can be made to the House of Delegates of the American Medical Association at its midwinter session Publication is about to be started in THE JOURNAL of state maps showing the distribution of physicians in 1947, and there will be published in this connection letters or excerpts from letters from each state concerning the need of physicians in the state. This material has been assembled by Mrs. M. Virginia Shuler, director of the Association's Bureau of Information.

In response to a question from Father Schwitalla, Dr. Mulholland informed the Committee that in Virginia, Kentucky and several other states scholarships are available to medical students who will promise to practice in rural areas in those states for a certain length of time. He said that the set-up in Virginia provides that a medical student will receive around $800 a year for each year in medical school.

Dr. Evans stated that the results of the undergraduate scholarships promoted by the Commonwealth Fund were not altogether satisfactory; a fair proportion of the men served the three years required of them in general practice in smaller communities and left as soon as their obligations were fulfilled. He went on to say:

The Commonwealth Fund plan required a two year internship, each one of which was tailor made so that the men had in their training everything needed to do a day by day job of medical practice. Some emergency surgical training was included, and immediately some of them set out to practice surgery. The program was discontinued a couple of years before the war. One of the problems encountered was that communities or areas to which the men went to practice were not places where they wanted to stay any longer than necessary in order to fulfil their obligations. However, they were given an opportunity to practice the kind of medicine they knew how to practice and an opportunity to make a respectable living. Those who stayed seem to be very happy. Many of the men who went to war asked to be relieved of their obligations when they returned.

Dr. Dearing stated that in Mississippi a student who acquires his medical education under a somewhat similar set-up cannot pay off his loan entirely except by giving service.

### RADIO BROADCASTING

Dr. W. W. Bauer, director of the Bureau of Health Education of the American Medical Association and supervisor of the Association's radio and television broadcasting programs, talked to the Committee as follows:

This subject may seem a bit remote from the tenor of the discussions this morning, but sooner or later decisions arrived at in meetings of this kind and the movements that proceed from them have to be interpreted to the public; radio and television are appropriate mediums for putting across these ideas. The television-listening public has almost doubled in the last six months.

Historically, the medical profession was among the early users of radio. The American Medical Association began broadcasting in Chicago on the network of the Columbia Broadcasting System as early as 1925 three times a day. Now we consider that one broadcast a week is a reasonable dose for the average listener. The radio industry is based on the Federal Communications Act, which empowers a U. S. government commission to license radio stations to use radio frequencies that are retained as public property. The radio stations are enjoined to broadcast "in the public interest and necessity." Radio stations are licensed as stations; networks are not. They are merely commercial devices for owning and operating or leasing stations. The theory of medical broadcasting has always been that it is a public service, and we have therefore approached the radio people with proposals that if they will furnish transmission service we will furnish everything else that goes into the program.

At first, all professional broadcasting consisted of talks by qualified speakers. For the most part, the radio medical talk has been rather dull. When a program does not interest the public, it does not interest the radio station operators. The changes that have come about in radio broadcasting have been on the side of presentation. We no longer rely on the talk to any extent. Unless there is a very able speaker available, we do not use the talk at all. We use now the interview and the radio drama. We have been accused of sacrificing professional dignity.

The American Medical Association now has two radio network programs. One of these is "Doctors Then and Now" and is broadcast on Saturday afternoons. This is a Centennial program honoring outstanding physicians of the past selected in each instance by the state medical society or by a group of state medical societies in a region. In each broadcast at the end of the dramatization of the life of the physician the program is switched to a local station, where a representative of the state medical association concerned speaks briefly on medical care in the state today. The other program, which is on the Mutual network, two hundred stations, can best be described by likening it to "One Man's Family." This program is called "Stephen Graham, Family Doctor," and emphasizes the role of the general practitioner.

We are preparing for the American Broadcasting System a program on mental hygiene exclusive of major psychoses, which will bring to the microphone twenty-six psychiatrists. In addition, we now have seventeen series of electrical transcriptions ranging all the way from a series on public health to one on mental hygiene. We find that the radio stations like these programs very much. They are distributed on a loan basis through state and county medical societies, emphasizing the fact that the service is from the local society.

### SHORTAGE OF NURSING PERSONNEL

Mr. Davis made the following statement:

As far as the American Hospital Association can ascertain, the number of nurses necessary for service to the nation is 360,000, 91,400 of whom are needed for private duty nursing. The figures developed show that 41,700 more nurses are needed; the actual shortage probably is some 60,000. The assumption that those who returned from service with the armed forces will reenter the civilian profession is not correct. Some of the reasons for the situation are: Before the war nurses worked a twelve hour day six days a week; now they work an eight hour day five days a week, which means that where 2.3 nurses were formerly required the same job now takes 4.3 nurses. The greatly increased number of hospital beds is another reason; in 1940 there were 1,226,000 hospital beds and in 1945 there were 1,738,000. There were 10 million patients in hospitals in 1940 and 16 million in 1945. There is a greater turnover of patients, which requires more nursing service. Last year not anywhere near as many student nurses were enrolled as in the year before. This year the American Hospital Association, in cooperation with the national nursing organizations, is working with the Advertising Council on a national recruitment program, which has already begun. Through the aid of the Advertising Council this program is receiving free advertising that would cost, if paid for at commercial rates, about $1,000,000.. The American Hospital Association has taken the initiative in trying to find the necessary 60,000 more nurses. It has contributed $10,000 to the campaign. The nursing schools have been asked to contribute, and the American Medical Associaion, the American College of Surgeons and some other national organizations have been approached. The com-

mittee that is carrying on the recruitment program hopes to be able to get 50,000 or 60,000 student nurses this year. The general impression around the country is that there will be more student nurses than there were last year.

In connection with the problem of the nurse shortage, there has been a great deal of discussion as to the desirability of producing more practical nurses. The professional nurses have raised their educational standards and perhaps are getting themselves out of bedside nursing. In Michigan the State Board of Education, in cooperation with the nursing organizations, has outlined a program by which six practical nurse training centers will be established in the larger cities patterned after a similar project that has been going on in Detroit for a number of years. These practical nurses will be recruited from the senior students in high schools. The teachers will be registered nurses on the high school faculties. We expect to start this program when the schools open in the fall. This is a part of the vocational education system. Under this program standards for practical nursing service will be established. It is considered that this type of nurse will be able to do from 80 to 90 per cent of the ordinary bedside nursing in hospitals.

A development which should receive consideration is the matter of the universities beginning to take over the education of registered nurses.

### REPORT OF SUBCOMMITTEE ON SPECIALTY BOARD FOR GENERAL PRACTITIONERS—CONTINUED

Drs. Bierring and Sensenich, members of the Subcommittee, and Miss Switzer, whose consultation they had requested, returned to the meeting and submitted the following report, which was adopted unanimously:

The Joint Committee for the Coordination of Medical Activities desires to record its recognition of the distinct contribution of specialty boards to the elevation of medical standards and the quality of medical practice in this country. However, the growing tendency to exclude the general practitioner from hospital staff privileges is having the effect of making it impossible for the general practitioner to secure the advantages of modern hospital facilities for the treatment of his patients. This is true in spite of the fact that by far the largest group of patients in the country relies on the general practitioner for medical services.

The Committee feels that there is need for a better understanding of the role of the general practitioner in medical service and, therefore, recommends a long range program on the part of all professional bodies concerned to this end.

The Committee does not believe the setting up of a specialty board for general practice meets the need at this time. However, there is immediate need for the integration of general practitioners into the hospital staffs throughout this country, and to accomplish this the Committee recommends that the Council on Medical Education and Hospitals of the American Medical Association develop as soon as possible several alternate plans.

The Committee further recommends that the American Medical Association and other professional organizations, as well as the national hospital associations, in their regional and annual meetings and in their publications give prominent place to a discussion of how this hospital staff integration can best be accomplished in order to make available for each eligible physician and his patients all the facilities provided for medical care in the community.

Mr. Davis discussed the subject as follows: With respect to the responsibility of the hospitals, I think it would be the general policy of the American Hospital Association to say that every reputable physician should have a hospital staff appointment. It seems to me that the whole problem at the present time stems from the fact that there is a maldistribution of physicians and also a shortage of hospital beds, particularly in the big cities. The physicians coming back from military service are crowding into the large cities, and that is where the problem exists. It does not exist outside the metropolitan areas. Hundreds of hospitals in this country have no specialists on their staffs. There is a hospital in Michigan where there are only two specialists, and the general practitioners are keeping out the specialists. A person who gets into a hospital ordinarily needs a specialist. The hospitals are confronted with the problem of providing to the public the highest possible quality of service.

### REPORT FROM LIAISON REPRESENTATIVE OF OFFICE OF THE SURGEON GENERAL

Colonel Armstrong brought to the attention of the Committee correspondence with young physicians, graduates of the Army Specialized Training Program, who are now in service. He said the letters follow a familiar pattern complaining about foreign duty, about lack of rotation between tactical units and hospitals and about the deferment of presently interning A. S. T. P. men when the writers are being held in service twenty-four months. Basically, he said, they reflect the fact that anything which has to do with military service at the moment is not popular.

Colonel Armstrong continued: These men cannot understand that they can learn something from sick call duty; those who are the least unhappy are those who are in a teaching hospital with a "Board" man as chief; some of the letters are from Korea, and many of the complaints from that theater are justifiable; General MacArthur has promised to investigate; the trouble is recognized and steps are being taken to correct it. The Office of the Surgeon General is "surplusing" every day; a check is kept on all theaters to see that the surplus is sent back.

The Chairman thanked Colonel Armstrong for his presentation.

### AMERICAN RED CROSS BLOOD BANK PROGRAM

Dr. Draper presented information concerning the Red Cross Blood Bank Program.

### TIME AND PLACE OF NEXT MEETING

It was voted to hold the next meeting at American Medical Association Headquarters in Chicago on Saturday morning, Aug. 16, 1947.

## Coming Medical Meetings

Conference of State Medical Society Secretaries and Editors, Chicago, A.M.A. Headquarters, Nov. 7-8. Dr. George F. Lull, 535 N. Dearborn St., Chicago 10, Secretary.

American Academy of Allergy, St. Louis, Hotel Jefferson, Dec. 15-17. Dr. Theodore L. Squier, 425 E. Wisconsin Ave., Milwaukee 2, Secretary.

American Academy of Dermatology and Syphilology, Chicago, Palmer House, Dec. 7-11. Dr. Earl D. Osborne, 471 Delaware Ave., Buffalo, N. Y., Secretary.

American Academy of Pediatrics, Dallas, Texas, Dec. 8-11. Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill., Secretary.

American Association of Railway Surgeons, Chicago, Nov. 23-25. Dr. Raymond B. Kepner, 547 West Jackson Boulevard, Chicago 6, Secretary.

American Otorhinologic Society for the Advancement of Plastic and Reconstructive Surgery, New York, Nov. 13. Dr. Norman N. Smith, 291 Whitney Ave., New Haven 11, Conn., Secretary.

American Society for the Study of Arteriosclerosis, Chicago, Hotel Knickerbocker, Nov. 2-3. Dr. O. J. Pollak, Wilmington General Hospital, Wilmington 14, Delaware, Secretary.

American Society of Anesthesiologists, New York, Hotel New Yorker, Dec. 4-5. Dr. Curtiss B. Hickcox, 745 Fifth Ave., Room 1503, New York 22, Secretary.

American Society of Clinical Pathologists, Chicago, Drake Hotel, Oct. 28-30. Dr. A. S. Giordano, 531 N. Main St., South Bend, Ind., Secretary.

American Society of Tropical Medicine, Atlanta, Ga., Dec. 2-4. Dr. Norman H. Topping, National Institute of Health, Bethesda 14, Md., Secretary.

Association of American Medical Colleges, Sun Valley, Idaho, Oct. 27-29. Dr. Fred C. Zapffe, 5 S. Wabash Ave., Chicago, Secretary.

Association of Military Surgeons of the United States, Boston, Hotel Statler, Nov. 13-15. Col. James M. Phalen, Army Medical Museum, Washington 25, D. C., Secretary.

Central Society for Clinical Research, Chicago, Drake Hotel, Oct. 30-Nov. 1. Dr. Ford K. Hick, 25 E. Washington St., Chicago 2, Secretary.

Indiana State Medical Association, French Lick, Oct. 28-30. Mr. Ray E. Smith, 23 E. Ohio St., Indianapolis 4, Executive Secretary.

New England Postgraduate Assembly, Boston, Copley-Plaza Hotel, Oct. 29-31. Dr. Leroy E. Parkins, 8 Fenway, Boston 15, Chairman.

New York State Association of Public Health Laboratories, Albany, Nov. 7. Miss M. B. Kirkbride, New Scotland Ave., Albany 1, Secretary.

Oklahoma City Clinical Society, Oklahoma City, Biltmore Hotel, Oct. 27-30. Dr. Elmer R. Musick, 512 Medical Arts Bldg., Oklahoma City, Director of Clinics.

Omaha Mid-West Clinical Society, Omaha, Oct. 27-31. Dr. John M. Thomas, 1031 Medical Arts Bldg., Omaha 2, Secretary and Director of Clinics.

Post Graduate Medical Assembly of South Texas, Houston, Texas, Coliseum, Dec. 1-3. Dr. E. Trowbridge Wolf, 229 Medical Arts Bldg., Houston, Texas, Secretary.

Puerto Rico, Medical Association of, San Juan, Dec. 10-14. Dr. Jeramfel Cordero, Box 3866, Santurce, Secretary.

Radiological Society of North America, Boston, Nov. 30-Dec. 5. Dr. Donald S. Childs, 607 Medical Arts Bldg., Syracuse 2, N. Y., Secretary.

Seaboard Medical Association of Virginia and North Carolina, Virginia Beach, Va., Dec. 2-5. Dr. Clarence Porter Jones, 3117 West Ave., Newport News, Va., Secretary.

Southern Medical Association, Baltimore, Nov. 24-27, Mr. C. P. Loranz, Empire Bldg., Birmingham 3, Ala., Secretary.

Southwestern Medical Association, Phoenix, Ariz., Hotel Westward Ho, Nov. 6-8. Dr. Louis W. Breck, 116 Mills St., El Paso, Texas, Secretary.

Southern Surgical Association, Hollywood, Fla., Dec. 9-11. Dr. Alfred Blalock, Johns Hopkins Hospital, Baltimore 5, Secretary.

Western Surgical Association, Colorado Springs, Broadmoor Hotel, Dec. 4-6. Dr. Warren H. Cole, 1853 West Polk St., Chicago 12, Secretary.

# GOVERNMENT SERVICES

## VETERANS ADMINISTRATION

### INTENSIVE RESEARCH ON HEART DISEASE

The Veterans Administration announces that intensive research in heart disease will be centered at the Mount Alto Hospital in Washington, D. C. The new research center, a part of which is already in operation, will conduct investigations on cardiovascular physiology and pathology for the primary purpose of improving the treatment of veterans. It will serve also as a training center for physicians by providing graduate study and resident training for certification by the American Board of Internal Medicine. The new center will provide consultation service in cardiovascular disease. The center will have the following eight major functions: treatment, clinical research, cardiovascular roentgenography, cardiac catheterization and hemodynamics, electrocardiography, pathology, statistical research and postgraduate teaching; later departments for research in biochemistry and biophysics will be added. The research center was developed under the supervision of Dr. George P. Robb, assistant medical director of the Metropolitan Life Insurance Company, who will continue as consultant to the cardiovascular research unit. Dr. Robb, a graduate of Indiana University School of Medicine, has conducted research projects at Harvard Medical School and New York University College of Medicine and during World War II was chief of the cardiovascular and electrocardiographic departments of Walter Reed General Hospital, Washington, D. C.

### DR. MAGNUSON APPOINTED CHIEF OF PROFESSIONAL SERVICES

The Veterans Administration announces the appointment of Dr. Paul B. Magnuson, Chicago, as acting chief of its Professional Services to succeed the late Brig. Gen. Elliott C. Cutler, who died August 16. Dr. Magnuson, formerly chairman, Department of Bone and Joint Surgery, Northwestern University Medical School, Chicago, came to the Veterans Administration in November 1945 on leave from Northwestern to assist the medical director in the reorganization of medical care for veterans. He has been with the Veterans Administration since then as acting chief of the Research and Education Service and will be succeeded in that position by Dr. Edward H. Cushing, former associate clinical professor of medicine, Western Reserve University, Cleveland, who has been associated with Dr. Magnuson as chief in that work.

## PUBLIC HEALTH SERVICE

### CANCER RESEARCH AND STUDY PROJECTS

The U. S. Public Health Service announced October 8 the award of more than $375,000 in grants for special research and study on improving technics for professional cancer instruction, a nationwide survey of cancer clinics and evaluation of cancer control measures. These awards, a part of the $14,000,000 cancer research and control program authorized by the last session of Congress, were reviewed and approved by the National Advisory Cancer Council, a nongovernmental committee of cancer specialists. Among the projects approved and the sums granted are the following:

Yale University School of Medicine, $25,000.00. Improvement of cancer teaching.

Washington University at St. Louis, $10,800.00. Experiment in medical education and oncology.

Medical College of the State of South Carolina, $21,800.00. Establishment of cancer control clinic, teaching and research.

Ohio State University College of Medicine, $24,800.00. Coordination of cancer teaching.

University of Chicago, $24,840.00. Development of research and teaching of cancer biology in a unit of oncology.

University of Tennessee, $24,035.40. Improvement and coordination of cancer teaching.

Tufts College, $24,820.00. Cancer control teaching.

Georgetown University, $24,500.00. Cancer teaching.

University of North Carolina, $3,400.00. Visual aids program for teaching pathology of neoplasms to medical students.

American College of Surgeons, $30,340.00. Survey of cancer clinics throughout the United States.

Tennessee Department of Public Health, $5,440.00. Epidemiologic and statistical research.

American Cancer Society, $36,600.00. Cooperative project for the production of diagnostic motion pictures.

Cornell University, $37,800.00. Establishment of a center for the study and instruction in the cytologic method for cancer diagnosis.

Maryland State Department of Health, $11,695.00. Evaluation of the cytologic test for cancer.

University of Minnesota, $21,250.12. Establishment of a model cancer detection center.

Georgetown University, $9,000.00. Follow-up studies of benign and malignant tumors.

University of Louisville, $7,000.00. Follow-up and analysis of cancer cases treated at Louisville General Hospital over the last twenty years.

Michigan Department of Health, $1,800.00. Training of pathologists in the technic of the cytologic test for cancer.

State Department of Health of Kentucky. Cytologic test training project, $2,250.00. Operation of a mobile diagnostic and treatment clinic, $11,700.00.

University of Tennessee, $4,878.48. Survey of the cytologic test for cancer in the city hospital.

## MISCELLANEOUS

### SALE OF SURPLUS GOVERNMENT PROPERTY

The War Assets Administration is conducting sales of surplus government property announced by the following regional offices. Physicians who are veterans have certain priorities in the purchase of surplus government property.

*Chicago.*—Sale of drugs, medicine and cosmetics. Beginning October 24 priority-registered hospitals may buy throughout October 30; wholesale and retail drug outlets and certified physicians may buy starting November 3. The property for sale is located in building 3212 B, Great Lakes, Ill.

*Seattle.*—Sale of drugs, bandages, splints and heating pads. Bids open November 7 for commercial buyers. No priority rights, as this property was previously offered to priority claimants. Bids must be received at the War Assets Administration Customer Service Center, 1409 Second Avenue, Seattle, before 11 a. m. November 7.

*St. Louis.*—Sale of drugs, medical supplies and equipment to priority claimants and commercial buyers to December 17. Bids may be sent to any WAA Customer Service Center (of which there is at least one in every state and in some states many). A deposit of 10 per cent of the total offering price must accompany each offer, and on any order exceeding $100,000 the customer must add 2 per cent of the amount of excess to the 10 per cent deposit required on smaller sums.

*Louisville.*—Sale of drugs, chemicals, surgical instruments, sterilizers, autoclaves, laboratory lamps, hospital equipment and supplies, and culture mediums and solutions. Sale opens to priority claimants only starting October 27. This sale is said to include $10,000,000 worth of government property with 1,800 different items from which to select. The Customer Service Center in Louisville is at 410 West Jefferson Street, but information can be obtained from any other Customer Service Center in the country.

# Medical News

**(Physicians will confer a favor by sending for this department items of news of general interest: such as relate to society activities, new hospitals, education and public health. Programs should be received at least two weeks before the date of meeting.)**

## CALIFORNIA

**Trichinosis and a Hamburger.**—The first case of trichinosis in Los Angeles County in two years was recently reported by the Los Angeles County Health Department. County food and drug inspectors found that the infected person had eaten raw hamburger ground in the same machine used for grinding pork and sausage.

**Symposium on Heart Disease.**—The Heart Division of the San Francisco Tuberculosis Association will present a symposium on heart diseases October 29 to November 1 at the St. Francis Hotel at 2 p.m. The first afternoon's program, sponsored by the American Academy of Pediatrics, Northern California, will be devoted to heart disease in children. Speakers from this state and guests from other parts of the country will take part in the program.

**Hospitals Merge to Form Medical Center.**—The merger of Mount Sinai Hospital, Los Angeles, and the Los Angeles Sanatorium at Duarte has been completed to form the Mount Sinai-Duarte National Medical Center. Directors of the hospitals will serve as associate directors in the same capacities they held previously. The Los Angeles Sanatorium has provided free care for the tuberculous poor since 1913, while Mount Sinai Hospital has been active since 1920 in caring for those suffering from chronic ailments. The Mount Sinai Clinic has offered additional services to the Los Angeles needy. The center is dedicated to providing medical care for those suffering from chest diseases, cancer, heart disease and other major illnesses. The Medical Center will create facilities for postgraduate medical education, a nurses' training school, medical research and eventually a medical school under Jewish auspices. New buildings under construction at Duarte will accommodate more than 700 patients.

## COLORADO

**Annual Meeting of the State Society.**—At the seventy-seventh annual session of the Colorado State Medical Society, September 17-20, the house of delegates adopted recommendations of its various committees, some of which follow:

1. The establishment of a statewide service for rehabilitation of civilians suffering physical handicaps, to provide for the nonmilitary victims care and rehabilitation equal to that now provided war veterans.
2. Revision and improvement of the whole field of neuropsychiatric care in the state.
3. Setting up a non-tax-supported, community operated and controlled child guidance center in Denver.
4. Approval of a six point program for the improvement of industrial health laws and services in the state with special consideration of the smaller, more widely dispersed industrial plants.
5. Approval of a seven point program for the improvement of rural health in the state with emphasis on expansion of the coverage of rural residents under Colorado Medical Service, Inc., the society-sponsored prepayment medical care plan.
6. Assumption of leadership toward establishment of scientifically planned health education in all levels of the state's educational system.
9. Expansion of Colorado Medical Service, Inc., from its present limited surgical care plan operations to include nonsurgical conditions.

The house of delegates created a Board of Supervisors, which will serve both in the general capacity of a "grand jury" and as a continuing study group to issue periodic advice to the members of the medical profession on matters of ethics and public conduct. It is empowered to receive complaints from physician and layman alike and, when justified, to prosecute charges against any erring physician before a local board of censors, the state Board of Councilors, the official Colorado State Board of Medical Examiners or any court. A temporary board of supervisors of twelve members, no two from the same component society, was nominated and elected to serve until a permanent board can take over under a constitutional amendment which will require one year to become effective. It was provided that no member of the board may participate in proceedings which affect a member of his own component society. The society voted also to join with the Colorado State Dental Association in cosponsorship of the proposal for establishing an approved school of dentistry in Colorado. There is no dental school in the Rocky Mountain region. The house of delegates directed that a new special committee be charged with the development of standards with which governmental and private agencies dealing with health and medical care problems must comply in order to obtain or maintain support of the medical profession. At this annual session the society awarded two special certificates, one to Dr. Florence R. Sabin, Denver, "for her life-long devotion to medical research and public health"; the other to Dr. Ella A. Mead, Greeley, in recognition of her more than twenty years of service as a member, and many times chairman, of the society's Board of Councilors. The following officers of the Colorado State Medical Society were installed: Drs. John S. Bouslog, Denver, president; Casper F. Hegner, Denver, president-elect, and George C. Shivers, Colorado Springs, treasurer.

## CONNECTICUT

**Yale Reorganizes Psychiatry Department.**—Complete reorganization of the department of psychiatry at Yale University School of Medicine, New Haven, with emphasis on the newest methods of treating mental illness, expanded instruction of medical students and residency training in cooperation with the Veterans Administration was announced October 2. Personnel changes include the appointment of Drs. Frederick C. Redlich, New Haven, executive officer of the department; Burness E. Moore, New Haven, physician-in-charge of the psychiatric inpatient clinic, and Richard J. Newman, Maryland, N. Y., physician-in-charge of the outpatient clinic. Dr. Lawrence S. Kubie, New York, has been appointed clinical professor of psychiatry; Dr. Robert P. Knight, Stockbridge, Mass., clinical professor, and Dr. Paul I. Yakovlev, Middletown, as associate clinical professor. The psychiatric inpatient clinic in the Yale Institute of Human Relations Building is in process of being completely renovated. Increasing emphasis will be placed in the clinic on the psychoneuroses and on psychosomatic disorders. Patients will be cared for jointly by the psychiatric staff and internists of the staff of the Yale School of Medicine and the New Haven Hospital. An individualized treatment program has been set up with major emphasis on psychotherapy, in which resident physicians will be carefully supervised. Two occupational therapeutists will be added to the staff. Yale Divinity School students will serve as male attendants in the wards as a part of their teaching program. Increasing emphasis will be placed on instruction of medical students in psychiatry. A new approach at Yale is the plan to help students to deal more adequately with psychiatric problems in general practice or in the specialties other than psychiatry. A new residency training program in neuropsychiatry, which will be under the Dean's Committee of the Veterans Administration, was started at Yale on October 1. A Veterans Administration contract clinic is presently operating in the psychiatric outpatient clinic. A Connecticut postgraduate seminar in neuropsychiatry has been organized and will be sponsored by the Joint State Hospital Committee and Yale. The psychiatry department will cooperate closely with the Yale Divinity School, Law School, Institute of Human Relations, the department of psychology, department of public health and the division of psychiatry of the Yale Department of University Health under Dr. Clements C. Fry.

## FLORIDA

**Four District Meetings.**—The Florida Medical Association has arranged four district meetings for its membership with programs beginning at 2:30 p.m. and ending with dinner.

Northwest Medical District, October 27, St. Andrews Bay Yacht Club, Panama City.

Southwest Medical District, October 29, Yacht and Country Club, Lakeland.

Southeast Medical District, October 30, New Fort Pierce Hotel, Fort Pierce.

Northeast Medical District, November 1, St. Augustine Country Club, St. Augustine.

Scientific assemblies and general sessions are included in the programs.

**Cancer Seminar at Jacksonville.**—A three day seminar on cancer will be held in Jacksonville November 12-14. There will be no registration fee. Funds for the project have been provided by the Florida Division of the American Cancer Society and the Florida State Board of Health. The Tumor Clinic of the Duval County Hospital initiated the project, and the physicians of Duval County will be the hosts. Invitations have been issued to all members of medical societies of the Southeastern states. Speakers will be:

Emil Novak, Baltimore, Tumors of the Female Genital Tract.
Samuel F. Marshall, Boston, Tumors of the Gastrointestinal Tract.
Archie L. Dean, New York, Tumors of the Genitourinary Tract.
Everett D. Sugarbaker, Jefferson City, Mo., Tumors of the Breast.
George T. Pack, New York, Mixed Tumors.
James E. Scarborough, Atlanta, Ga., Tumors of the Head and Neck.
Herbert D. Adams, Boston, Tumors of the Chest.
Roscoe R. Spencer, Bethesda, Md., Cancer Research.
Everett L. Bishop, Atlanta, Ga., Tumor Pathology.

## ILLINOIS

**Graduate Conference at Rockford.**—The Illinois State Medical Society has arranged a postgraduate conference for the First Councilor District at the Hotel Faust, Rockford, November 5, beginning at 1:30 p.m. and extending into the evening. Seven Chicago physicians will speak on coronary disease, hypertension, congenital heart deformity, kidney diseases, fracture problems and peptic ulcer.

**Annual Conference on Exceptional Children.**—The State Commission for Handicapped Children will sponsor the fourth annual Governor's Conference on Exceptional Children, to be held in Springfield, October 24, at the Leland Hotel. The conference will give an opportunity for first hand observation of methods in educational rehabilitation of handicapped children. Any one interested is invited to attend. Speakers on the program include: Dr. Roland R. Cross, director, Illinois Department of Public Health, Springfield; Morton A. Seidenfeld, Ph.D., director of psychologic services, National Foundation for Infantile Paralysis, New York; Dr. Francis N. Brill, orthopedic surgeon of Springfield, and Howard E. M. Miller, executive director, Illinois Commission for Handicapped Children, Chicago.

### Chicago

**Narcotic Violation.**—Dr. Chester A. Price, 6345 University Avenue, Chicago, pleaded nolo contendere to an indictment charging violation of the Federal Narcotic Law and on September 4 was sentenced to a term of one year and one day.

**Course in Electrocardiographic Interpretation.**—A course in electrocardiographic interpretation for graduate physicians will be given at the Michael Reese Hospital Postgraduate School by Dr. Louis N. Katz, director of cardiovascular research. The class will meet each Wednesday from 7 to 9 p.m. for twelve weeks, beginning Feb. 17, 1948. Information may be obtained from the Office of the Dean, Michael Reese Hospital Postgraduate School.

**University Course in Allergy.**—A twelve month graduate course for clinical training and research in allergy is being offered by the University of Illinois allergy unit, a joint organization of the colleges of medicine and pharmacy, during the 1947-1948 school year. The course, open to six physicians, is designed to train specialists in allergy to help alleviate the shortage of allergists in the country. Though primarily clinical in scope, the course will include instruction in basic subjects related to allergy. The training and research program will be correlated with the university's allergy clinic. Registration was conducted October 1.

## INDIANA

**Honor Peru's Fifty-Year Physicians.**—The Eleventh District Medical Association at a banquet September 17 in Peru honored Drs. Frank M. Lynn, David C. Ridenour and John E. Yarling, all of Peru, who have been in practice more than fifty years. Dr. Edgar F. Kiser, Indianapolis, was the principal speaker.

**Testimonial Dinner to Dr. Sensenich.**—A testimonial dinner in honor of Dr. Roscoe L. Sensenich, President-Elect of the American Medical Association, was held October 8 at the Indiana Club, South Bend, under the auspices of the St. Joseph County Medical Society, of which he is a member. Dr. Harold D. Pyle, president, presided. The after dinner address was given by Dr. Morris Fishbein, Chicago, Editor of THE JOURNAL, on medical statesmanship. Dr. Robert B. Sanderson, South Bend, presented a scroll to Dr. Sensenich. Other speakers were Dr. Floyd H. Romberger, president, Indiana State Medical Association, and Drs. Ernest R. Irons, Chicago, Secretary, and Elmer L. Henderson, Louisville, Ky., Chairman, Board of Trustees, American Medical Association.

**Division of Venereal Disease Control.**—Dr. Carl C. Kuehn, Indianapolis, formerly with the U. S. Public Health Service, has been placed in charge of venereal disease control activities of the state board of health, succeeding Dr. George W. Bowman, Indianapolis, who is being loaned to the Indianapolis City Board of Health to help with venereal disease control and continue his work at the rapid treatment center. A graduate of Indiana University School of Medicine, Bloomington-Indianapolis, 1941, Dr. Kuehn attended the school of public health at the University of Michigan, Ann Arbor, and received his master's degree in public health last spring. Dr. C. Merle Bundy, Indianapolis, who for the last year has been acting director of the division of tuberculosis control on loan from the U. S. Public Health Service, has decided to resign from the Service and remain in the state. He is a graduate of the Indiana University School of Medicine, 1942.

## KENTUCKY

**State Medical Election and Awards.**—At the annual meeting of the Kentucky State Medical Association September 29-October 2, Dr. J. Garland Sherrill, Louisville, received the association's Distinguished Service Medal for pioneering in the use of spinal anesthesia. Dr. J. Duffy Hancock, a member of the surgical faculty of the University of Louisville School of Medicine, Louisville, since 1923, from which school he graduated in 1921, received the E. M. Howard Medal for outstanding services as a physician and surgeon. The association installed Dr. Guy Aud, Louisville, as president and chose Dr. Charles A. Vance, Lexington, president-elect.

## MICHIGAN

**Typhoid at Saginaw Checked.**—Typhoid fever, which 12 persons of Saginaw contracted in September, has been traced to a contaminated surface well, according to Dr. Frederick S. Leeder, Lansing, director of the state health department's bureau of epidemiology. The well apparently was contaminated by the discharge from a septic tank, and the carrier is being sought.

## NEBRASKA

**Creighton University Appointments.**—Among the recent appointments to the faculty of the Creighton University School of Medicine, Omaha, are: assistant professor of bacteriology, James M. Beebe, Ph.D., Amherst, Mass.; assistant professors of physiology and pharmacology, Harold C. Struck, Ph.D., Chicago, and John Ferguson, Ph.D., Edmonton, Alberta, Canada; instructor in pathology, Dr. F. J. Campos, El Paso, Texas; assistants in surgery, Drs. Robert Fitzgibbons, William N. Hardman, both of Rochester, Minn., in charge of anesthesiology, and Harry H. McCarthy, Rochester, Minn.; assistant in medicine, Dr. John D. Hartigan, Rochester, Minn.; acting assistants in medicine, Drs. Richard J. Fangman and William O. Griffith, Council Bluffs, Iowa.

## NEW YORK

**Graduate Instruction for County Societies.**—The Medical Society of the State of New York and the New York State Department of Health have arranged postgraduate instruction for the following county medical societies:

Clinton County, December 18 at 8 p. m. in the Champlain Valley Hospital Nurses Home, Plattsburg, on arthritis.
Jefferson County, November 13 at 8:30 p. m. at the Woodruff Hotel, Watertown, on medical aspects of the atomic bomb.

**Appoint Director of Public Health Education.**—Dr. Granville W. Larimore, New York, has been appointed director of the Office of Public Health Education, State Health Department, succeeding Mr. Bert R. Rickards, who served for thirty years (THE JOURNAL, Feb. 8, 1947, page 413). Dr. Larimore comes to the department from the American Cancer Society, where he had been educational director. He received his M.D. degree from Rush Medical College of the University of Chicago in 1936 and a Master of Public Health from Harvard University in 1942. During the War he served as chief of the army's health education branch, venereal disease control division.

### New York City

**Lectures for Laymen.**—The New York Academy of Medicine will inaugurate the thirteenth series of its Lectures to the Laity with the Linsly R. Williams Memorial Lecture to be delivered October 30 at 8:30 p.m. by Lewis L. Strauss, New York, member of the U. S. Atomic Energy Commission, on "The Atom in Civil Life." On November 1 Dr. George R. Hargreaves, London, will speak on "Psychology of Leadership in War and Peace." The third lecture will be the ninety-eighth anniversary discourse of the New York Academy of Medicine, to be given by Sir Raphael Cilento, director of social activities, United Nations, Lake Success, N. Y., on "Food and Civilization."

**Hospital Physicians Added to University Staff.**—Eleven staff members of hospitals have received academic appointments at Columbia University College of Physicians and Surgeons as a result of the university's recently announced plan of affiliation with St. Luke's Hospital and Mary Imogene Bassett Hospital in Cooperstown (THE JOURNAL, Aug. 23, p. 1496). Dr. William F. MacFee, director of surgery at St. Luke's, was named clinical professor of surgery. Assistant professors of surgery are Drs. Benjamin Shore Jr. and Paul C. Morton; assistant clinical professors of medicine, Drs. John J. Keating, Albert C. Herring and Waldo B. Farnum. Staff members of the Goldwater Memorial Hospital, Welfare Island, who received appointments are Drs. Margaret Bevans and Robert W. Berliner. At the Mary Imogene Bassett Hospital Dr. James Bordley III was appointed associate clinical professor of medicine and Dr. Monroe A. McIver, associate clinical professor of surgery.

**Cancer Detection Center Opened.**—The first Cancer Prevention and Detection Center to be operated by the city health department has been opened at the Kips Bay-Yorkville Health Center, 411 East Sixty-Ninth Street. The center is a cooperative project sponsored by the city health department, the New York City Cancer Committee, Cornell University Medical College and the Strang Cancer Prevention Clinic of Memorial Hospital for the Treatment of Cancer and Allied Diseases. Operation of this center, planned by the health department as the first of several, will determine the most effective way to administer such programs. The New York City Cancer Committee will supply funds for professional personnel and special services for the first year of operation. The objective is to determine those persons who show symptoms for which diagnostic investigation is indicated. Treatment will not be given, and the detection service will be free. The center will be open to presumably well adults regardless of age. However, chief attention will be directed to persons over 40 years of age who are referred either by their physician or some medical service, or who may come without referral. Patients giving indications of any condition requiring medical attention will be referred to their physicians or to an appropriate clinic. Dr. Emerson Day of Cornell University Medical College will direct the cancer center. The health department is furnishing space, nursing and secretarial service and laboratory, dental and x-ray facilities. Staff members of the New York and Memorial hospitals will serve as consultants on special cases. An advisory committee of the sponsors will determine the general policies governing the clinic and select the medical personnel.

## OHIO

**Research on Radioactive Substances.**—Under a $100,000 grant from the U. S. Atomic Energy Commission, Western Reserve University School of Medicine, Cleveland, will conduct research on the effects of radioactive substances and atomic energy on the body and on living cells. Dr. Hymer L. Friedell, professor of radiology, will direct the project and Dr. Arnold D. Welch, head, department of pharmacology, and Harland G. Wood, Ph.D., head, department of biochemistry, will be consultants. Paul A. Mattis, Sc.D., former professor of pharmacology, University of Florida School of Pharmacy, now at the Western Reserve School of Pharmacy, will direct the pharmacologic division of the project. Dr. Paul S. Lavik, assistant professor of biochemistry in the school of medicine, will study the effects of radioactive elements on enzymes and will supervise the work of the biochemical division. This research will be related to that conducted in several other institutions by the Atomic Energy Commission.

## OREGON

**Narcotic Violation.**—Dr. Philip L. Newmyer, Portland, who was arrested May 9 and freed on $2,500 bond, was fined $5,000 in federal court when found guilty on six counts charging him with violating the Federal Narcotics Act by the sale of morphine tablets not in the course of his professional practice.

**First Woman Elected President.**—At the annual session of the Oregon State Medical Society in Portland, September 4-6, Dr. James C. Hayes, Medford, was installed as president. Dr. Leslie S. Kent, Eugene, was made president-elect; Dr. Werner E. Zeller, Portland, secretary, and Dr. Roger H. Keane, Portland, treasurer. Dr. Kent is the first woman to be chosen to head a state medical association. Dr. Kent, whose father and late husband were physicians, received her M.D. degree from Lincoln Medical College, Lincoln, 1917. In 1923 she began practice in Eugene. She is a former president of the Lane County Medical Society.

## PENNSYLVANIA

**State Medical Election.**—At the annual session of the Medical Society of the State of Pennsylvania, September 15-18, Dr. Elmer Hess, Erie, was installed as president. Dr. Gibson C. Engel, Philadelphia, was chosen president-elect and Dr. Walter F. Donaldson, Pittsburgh, was reelected secretary-treasurer for the twenty-ninth consecutive year.

**A Series of Graduate Courses.**—The medical society of the state of Pennsylvania in cooperation with the medical schools of the state has arranged a series of graduate refresher courses to be held from October through May for general practitioners. Physicians may select one of the following centers: Allentown, Harriburg, Johnstown, Oil City, Wilkes-Barre or Williamsport. Each day of instruction will consist of eight hours. Emphasis will be placed on physiologic and pharmacologic points of view. Subjects to be covered are febrile diseases and endocrinology, cardiovascular diseases, neuropsychiatry, skeletal and muscular diseases, hematology and metabolic disorders, skin diseases and nutrition, urology, gynecology and obstetrics, respiratory diseases and anesthesiology, gastroenterology and modern therapy. The schedule is so arranged that a registrant who is unable to attend a particular session at his own center will be able to attend an identical session by traveling to a neighboring center on another date. The registration fee for members of the state society is $25; for nonmembers, $50. Information may be obtained from the Committee on Graduate Education, 230 State Street, Harrisburg.

## WEST VIRGINIA

**Pediatric Consultant.**—Dr. Henrietta L. Marquis, Charleston, has been appointed as part time pediatric consultant to the division of maternal and child health. Before moving to Charleston in 1946, Dr. Marquis practiced pediatrics at Beckley. She has participated in the child health program of the state health department since 1935 and has served as a clinician at the Well-Child Conference in Beckley.

**Hospital Advisory Board.**—A seven member hospital-licensing advisory board has been appointed by the governor under the provisions of the hospital-licensing act passed by the legislature this year. The members will serve as consultants to the commissioner of health in issuing licenses to hospitals, sanatoriums, nursing homes and related institutions. The board is composed of John S. Alfriend, Charles Town; Charles Warner and C. R. Adams, Charleston; Dr. Hu C. Myers, Philippi; J. S. Turk, Wheeling; Sister M. Carola, Huntington, and James L. Foster, Bluefield.

## WISCONSIN

**Dr. Hirschboeck Appointed Dean.**—Dr. John S. Hirschboeck, a member of the faculty of Marquette University School of Medicine, Milwaukee, since 1939, was appointed dean of the school September 28, to succeed the late Dr. Eben J. Cary. He was graduated from Marquette University School of Medicine in 1937, and in 1941 he received a degree of master of science, specializing in hematology. He served in the Navy from Dec. 14, 1941 to 1945.

**Walter Zeit to Head of Department of Anatomy.**—Walter Zeit, Ph.D., who has been an associate professor of anatomy at Marquette University School of Medicine, Milwaukee, since 1943, has been appointed director of the department to succeed the late Dr. Eben J. Carey. Dr. Zeit received his Ph.D. degree from Marquette University in 1939 and has been on the staff of the School of Medicine since 1921, having been an assistant in anatomy as an undergraduate.

## GENERAL

**Diploma Lost.**—The diploma of Dr. Collins Fremont Hall, who graduated from Duke University School of Medicine, Durham, N. C., on June 6, 1938, has been lost. A duplicate is being issued by Duke to Dr. Hall.

**International College Dedicates Home.**—The United States Chapter of the International College of Surgeons dedicated its new home office at 1516 Lake Shore Drive, Chicago, at a program October 2. Dr. Raymond W. McNealy, Chicago, was general chairman of the program, and Dr. Herbert Acuff, Knoxville, Tenn., presided.

**Central Society for Clinical Research.**—The Society for Clinical Research will hold its twentieth annual meeting October 31-November 1 at the Drake Hotel, Chicago, under the presidency of Dr. Carl V. Moore, St. Louis. Numerous short papers will be presented by speakers from various sections of the country. There will not be exhibits or a social program.

**Dr. Eusterman Receives Friedenwald Medal.**—Dr. George B. Eusterman, Mayo Clinic, Rochester, Minn., was the recipient of the Friedenwald Medal given at the annual meeting of the American Gastro-Enterological Association in Atlantic City, N. J., in June for his outstanding work in gastroenterology. The July issue of *Gastroenterology* was dedicated to Dr. Eusterman.

**Dr. Perkins Named Director of National Tuberculosis Association.**—Dr. James E. Perkins, Albany, deputy commissioner, New York State Health Department, on Jan. 1, 1948 will succeed Dr. Kendall Emerson, New York, retired, as managing director of the National Tuberculosis Association. Dr. Perkins has been connected with the New York State Department of Health since 1934, when he joined the staff as an epidemiologist. He was last year appointed deputy commissioner. Dr. Emerson, managing director since 1928, has agreed to remain a consultant to the association.

**Military Surgeons Meeting.**—The Association of Military Surgeons of the United States will hold its annual convention at the Hotel Statler, Boston, November 13-15, under the presidency of Dr. Warren F. Draper, Washington. The program is made up of lectures on atomic energy, aviation medicine, preventive and environmental medicine; current personnel problems, psychiatry, research and development, dentistry and veterinary medicine, medicine and surgery, and panel discussions on the Army Nurse Corps, aviation medicine, dentistry and the Medical Service and Sanitary corps.

**Annual Meeting of Clinical Pathologists.**—The annual meeting of the American Society of Clinical Pathologists will be held at the Drake Hotel, Chicago, October 27-30 with demonstrations at the University of Illinois College of Medicine and its Research and Educational Hospitals, Mt. Sinai Hospital and Hektoen Institute. The program includes a symposium on cardiolipin antigen and a seminar on Thursday on diseases of the kidney. There will be technical and scientific exhibits. At the banquet October 29 Dr. Edward L. Bortz, Philadelphia, President, American Medical Association, will speak on "Medicine's New Frontiers."

**Prevalence of Poliomyelitis.**—Reports of cases of poliomyelitis for the periods indicated have been received from the division of public health methods, U. S. Public Health Service:

| Division and State | Week Ended Oct. 11, 1947 | Week Ended Oct. 12, 1946 | Week Ended Median, 1942-1946 | Total to Oct. 11, 1947 | Total to Oct. 12, 1946 | Total * March 16-Oct. 11, 1947 | Total * March 17-Oct. 12, 1946 |
|---|---|---|---|---|---|---|---|
| **New England:** | | | | | | | |
| Maine | 2 | 3 | 3 | 37 | 26 | 34 | 26 |
| New Hampshire | 0 | 4 | 1 | 22 | 136 | 18 | 135 |
| Vermont | 0 | 6 | 2 | 28 | 37 | 20 | 33 |
| Massachusetts | 24 | 32 | 27 | 299 | 239 | 292 | 235 |
| Rhode Island | 4 | 9 | 1 | 134 | 75 | 133 | 75 |
| Connecticut | 8 | 17 | 9 | 127 | 82 | 124 | 74 |
| **Middle Atlantic:** | | | | | | | |
| New York | 61 | 77 | 68 | 958 | 1,102 | 922 | 1,069 |
| New Jersey | 9 | 13 | 14 | 242 | 201 | 236 | 195 |
| Pennsylvania | 30 | 12 | 12 | 372 | 217 | 358 | 205 |
| **East North Central:** | | | | | | | |
| Ohio | 88 | 14 | 14 | 1,119 | 582 | 1,109 | 567 |
| Indiana | 15 | 23 | 5 | 202 | 306 | 186 | 301 |
| Illinois | 29 | 139 | 48 | 730 | 2,060 | 708 | 2,052 |
| Michigan | 31 | 57 | 22 | 531 | 769 | 507 | 761 |
| Wisconsin | 15 | 67 | 13 | 178 | 1,011 | 154 | 998 |
| **West North Central:** | | | | | | | |
| Minnesota | 3 | 67 | 16 | 195 | 2,594 | 182 | 2,593 |
| Iowa | 12 | 39 | 18 | 142 | 475 | 134 | 466 |
| Missouri | 7 | 70 | 6 | 106 | 1,053 | 96 | 1,046 |
| North Dakota | 0 | 14 | 1 | 68 | 415 | 63 | 415 |
| South Dakota | 1 | 6 | 1 | 12 | 344 | 10 | 344 |
| Nebraska | 10 | 44 | 7 | 178† | 503 | 171† | 502 |
| Kansas | 4 | 71 | 11 | 84 | 846 | 66 | 842 |
| **South Atlantic:** | | | | | | | |
| Delaware | 0 | 4 | 2 | 126 | 26 | 126 | 26 |
| Maryland | 7 | 2 | 2 | 85 | 78 | 79 | 76 |
| District of Columbia | 4 | 1 | 1 | 18 | 23 | 16 | 22 |
| Virginia | 12 | 4 | 5 | 138 | 95 | 128 | 89 |
| West Virginia | 10 | 4 | 2 | 106 | 63 | 102 | 60 |
| North Carolina | 18 | 3 | 3 | 182 | 104 | 167 | 97 |
| South Carolina | 5 | 0 | 0 | 28† | 19 | 27† | 16 |
| Georgia | 2 | 1 | 1 | 67 | 136 | 60 | 128 |
| Florida | 8 | 11 | 3 | 85 | 523 | 60 | 474 |
| **East South Central:** | | | | | | | |
| Kentucky | 7 | 1 | 2 | 85 | 99 | 84 | 96 |
| Tennessee | 8 | 4 | 5 | 114 | 147 | 102 | 138 |
| Alabama | 2 | 1 | 1 | 46 | 358 | 33 | 355 |
| Mississippi | 1 | 12 | 1 | 43 | 271 | 26 | 254 |
| **West South Central:** | | | | | | | |
| Arkansas | 3 | 10 | 3 | 72 | 338 | 61 | 326 |
| Louisiana | 0 | 9 | 1 | 44 | 327 | 26 | 308 |
| Oklahoma | 0 | 17 | 11 | 43 | 331 | 32 | 325 |
| Texas | 0 | 21 | 20 | 155 | 846 | 130 | 818 |
| **Mountain:** | | | | | | | |
| Montana | 1 | 5 | 1 | 24 | 114 | 22 | 98 |
| Idaho | 50 | 4 | 1 | 195 | 35 | 185 | 35 |
| Wyoming | 1 | 2 | 2 | 16 | 112 | 13 | 111 |
| Colorado | 3 | 21 | 3 | 53 | 855 | 48 | 854 |
| New Mexico | 2 | 5 | 0 | 32 | 151 | 29 | 150 |
| Arizona | 0 | 4 | 1 | 28 | 103 | 25 | 100 |
| Utah | 0 | 3 | 3 | 10 | 118 | 5 | 112 |
| Nevada | 0 | 0 | 0 | 1 | 3 | 1 | 3 |
| **Pacific:** | | | | | | | |
| Washington | 10 | 36 | 14 | 118 | 396 | 110 | 363 |
| Oregon | 10 | 8 | 8 | 71 | 134 | 66 | 130 |
| California | 23 | 65 | 30 | 705 | 1,808 | 556 | 1,721 |
| Total | 540 | 1,042 | ... | 8,454† | 20,686† | 7,842† | 20,219 |
| Median, 1942-1946 | ... | .... | 549 | 10,845 | | 10,448 | |

* Last two columns show reported incidence since approximate seasonal low week (week ended March 15 to 21).

† Figures changed by corrected reports.

**Survey of Food and Nutrition Research.**—A national survey of activities in the field of food and nutrition research is being undertaken by the Food and Nutrition Board of the National Research Council with the support of the Quartermaster Food and Container Institute of the armed forces. Leaders in the field have expressed a need for a central register of food and nutrition research to facilitate the coordination of peacetime research in relation to national security and public welfare. The register will serve as a basis for rapid mobilization of food research resources in event of national emergency. The survey will cover the chemical, physiologic, microbiologic, technologic, psychologic and basic economic studies of nutrition research. Correlation of such studies with regard to health, acceptability, stability, utility and economy of food will be made. Subject listings of research and progress pertaining to foods and nutrition are being obtained from directors of research in industry, universities, government and other agencies, foundations, public trusts and industry. In addition, a roster of personnel engaged in research is being developed in collaboration with the Office of Scientific Research of the Research Council. Charles G. King, Ph.D., Scarsdale, N. Y., scientific director of the Nutrition Foundation, is chairman of the committee on survey of food and nutrition research, which will supervise the project and make reports. Information may be obtained from the office of the Food and Nutrition Board of the National Research Council, 2101 Constitution Avenue, Washington, D. C.

## AUSTRALIA

**Flying Doctor Service.**—From eight bases throughout Australia the flying doctor service brings medical aid to families and sheep ranchers in Australia's "outback." Each base, according to the Associated Press, has a physician, pilot and radio operator, and a two way radio and twin engined airplane fitted out as an ambulance. People on isolated farms contact the base with a "pedal wireless," which can be installed in homes for $275. Medical advice for mild illnesses is given from the base by radio with instructions for the use of a medical kit with which every home is equipped. If a patient needs hospital attention he is flown back to the base in the aerial ambulance. The service is maintained by government subsidy, private donations and a voluntary contribution scheme by which settlers pay a yearly subscription. Nonsubscribers receive free medical advice by radio but are expected to pay for a doctor's call. Charges are based on the average carrying capacity of the property and range from $16 for property with three thousand sheep to $65 for property with seventeen thousand sheep. Dr. John Flynn, superintendent of the Presbyterian Inland Mission, began the service twenty-six years ago with one base at Cloncurry in North-West Queensland.

## EGYPT

**Cholera in Egypt.**—According to the Associated Press, the death toll in the three week cholera epidemic in Egypt had reached 2,128 by October 19. On the preceding day the health ministry listed 247 deaths in the twenty-four hours ending at 8 a. m. A specially equipped plane of the United States air force arrived in Cairo October 19 from Frankfort, Germany, with 100,000 gallons of DDT spraying mixture to combat flies spreading the disease. It is expected that the plane will be used to reach distant areas while smaller aircraft continue to spray Cairo and the nearby region.

# Marriages

TRUMAN G. SCHNABEL Jr., Philadelphia, to Miss Mary Florence Hyatt of Washington, Ind., in New York, September 13.

GEORGE LOUIS ARMBRECHT to Miss Eleanor Lincoln Flint, both of Wheeling, W. Va., September 30.

RICHARD LORD [illegible]LEY, New York, to Miss Mary Catesby Jones of Petersham, Mass., September 6.

KENNETH SIHLER SHEPARD, Washington, D. C., to Miss Helen Reis of Evanston, Ill., recently.

JOHN M. KELLER, Philadelphia, to Miss Ruth Clare Stranford of Ashland, N. J., September 26.

FRANCES A. SWAN, Livonia, N. Y., to Mr. Walter H. Lieneck of Brooklyn, August 16.

JOHN HORTON DOANE JR., Sayre, Pa., to Miss Hilda Mann Hogg of Towanda, August 23.

ANSON G. HURLEY to Miss Betty Pheneger, both of Muncie, Ind., September 6.

# Deaths

**Barney James Hein** ✠ Toledo, Ohio; born in Toledo on April 23, 1889; Toledo Medical College, 1912; specialist certified by the American Board of Orthopaedic Surgery; member of the House of Delegates of the American Medical Association since 1939; member of the Clinical Orthopaedic Society and the American Academy of Orthopaedic Surgeons; fellow of the American College of Surgeons; president of the Ohio State Medical Association, 1938-1939, and for three terms served as councilor of the Fourth District, in which position he was active on various committees; chairman of the committee on public relations and economics since 1940; a member and formerly chairman of the committee on industrial health and workmen's compensation; member of the board of directors of Ohio Medical Indemnity, Inc., the association's prepayment medical care plan; president of the Academy of Medicine of Toledo and Lucas County in 1930; during World War I served overseas in charge of the orthopedic department of Evacuation Hospital number 5 and saw active service in Aisne-Marne, Oise-Aisne, St. Mihiel, Meuse, Argonne and Ypres-Lys engagements; following duty at Orthopedic Base Hospitals number 9 and 11 was discharged as a captain in March 1919; director of the orthopedic staff at St. Vincent's Hospital and member of the orthopedic staffs at Toledo, Flower, Riverside and Lucas County General hospitals; served as trustee for the Toledo Newsboy's Association (later the Boys' Club of Toledo), the Toledo Hospitalization Association, Toledo Society for Crippled Children, Toledo Chamber of Commerce and the Toledo Medical College Fund of Toledo University; served on the advisory board of the University of Toledo's athletic department; charter member and past president of the Lion's Club of Toledo; died August 17, aged 58.

**James A. Abney,** Brownwood, Texas; Galveston Medical College, 1871; Confederate veteran; died July 29, aged 100, of senility.

**John Pelham Bates,** Greenwood, Miss.; Vanderbilt University School of Medicine, Nashville, Tenn., 1896; on the staff of the Greenwood Leflore Hospital, where he died August 8, aged 79, of myocarditis.

**Franklin Carlisle Bivings,** Atlanta, Ga.; University of Illinois College of Medicine, Chicago, 1916; served during World War I; on the staff of St. Joseph's Infirmary, where he died August 7, aged 68, of coronary heart disease.

**Frank Brostrom** ✠ New Orleans; Jefferson Medical College of Philadelphia, 1923; affiliated with Touro Infirmary and the New Orleans Hospital and Dispensary for Women and Children; died July 31, aged 53, of coronary thrombosis.

**Henry M. Brown,** Roswell, N. M.; Chicago Medical College, 1892; died in Colorado Springs July 31, aged 80, of coronary thrombosis.

**Henry Campbell,** Graham, Mo.; Kentucky University Medical Department, Louisville, 1903; died in St. Francis Hospital, Maryville, July 29, aged 67, of cerebral hemorrhage.

**Lewis Richard Carr,** Wayne, Ohio; Ohio State University College of Medicine, Columbus, 1916; past president of the Academy of Medicine of Toledo and Lucas County; served during World War I; formerly on the staff of the Flower Hospital in Toledo; member of the Clinical Orthopaedic Society and the American Academy of Orthopaedic Surgeons; died July 31, aged 56, of cerebral hemorrhage.

**Frank Elijah Chapman,** Montgomery, Ala.; Louisiana State University School of Medicine, New Orleans, 1937; member of the American Medical Association; formerly affiliated with the Pines Sanatorium in Shreveport, La.; served with the division of tuberculosis control of the state department of public health; died in Grove Hill August 19, aged 34, of tuberculosis.

**William Stewart Chapman,** Jackson, Ala.; Emory University School of Medicine, Atlanta, Ga., 1924; member of the American Medical Association; past president of the Clarke County Medical Society; councilor of the Medical Association of the State of Alabama; died July 22, aged 50, of coronary occlusion.

**George William Cline,** Muncie, Ind.; Indiana University School of Medicine, Indianapolis, 1941; member of the American Medical Association; interned at the Eloise Hospital and Infirmary in Eloise, Mich.; served a residency at the Logansport State Hospital in Logansport, Ind.; died in the Union City Hospital in Union City, July 6, aged 33, of cerebral hemorrhage.

**Manning E. Cohn,** Cleveland Heights, Ohio; Ohio State University College of Medicine, Columbus, 1933; member of the American Medical Association; served during World War II; died in the Mount Sinai Hospital in Cleveland July 11, aged 39, of coronary thrombosis.

**James Joseph Collins,** Woodbridge, N. J.; Long Island College Hospital, Brooklyn, 1907; died June 19, aged 70, of hypertension, diabetes mellitus and a fractured femur received in a fall.

**Francis Joseph S. Conlan** ✠ San Francisco; Rush Medical College, Chicago, 1899; member of the Pacific Coast Oto-Ophthalmological Society; fellow of the American College of Surgeons; on the staff of St. Mary's Hospital, where he died July 17, aged 73, of coronary heart disease.

**Paul James Connor** ✠ Denver; University of Texas School of Medicine, Galveston, 1912; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; past president of the state board of health; served during World War I and as president of the staff of the Presbyterian Hospital; affiliated with St. Luke's Hospital, where he died July 26, aged 60, of heart disease.

**Charles Eli Cottingham,** Indianapolis; Medical College of Indiana, Indianapolis, 1895; member of the American Medical Association; served on the faculty of the Indiana University School of Medicine and on the staffs of the Richmond (Ind.) State Hospital, James Whitcomb Riley, City, St. Vincent's and Methodist hospitals; died July 23, aged 78, of coronary thrombosis.

**William Allen Cracraft Jr.,** Wheeling, W. Va.; University of Virginia Department of Medicine, Charlottesville, 1901; member of the American Medical Association; served in France during World War I; on the staff of the Ohio Valley General Hospital, where he died July 10, aged 69, of hypertensive heart disease.

**Herbert William Emerson,** Ann Arbor, Mich.; University of Michigan Medical School, Ann Arbor, 1915; member of the American Medical Association; served on the faculty of his alma mater; died in the Hamilton General Hospital, Hamilton, Ontario, Canada, June 21, aged 66, of cerebral hemorrhage.

**Charles Fox Gardiner,** Colorado Springs, Colo.; Bellevue Hospital Medical College, New York, 1882; member of the American Medical Association and the American Clinical and Climatological Association; affiliated with the Beth-El Hospital; author of "Doctor at Timberline"; died July 31, aged 89, of myocarditis.

**Harold Eugene Gibson** ✠ Kenton, Ohio; Eclectic Medical College, Cincinnati, 1915; served in France during World War I; past president of the Hardin County Medical Society; died suddenly, July 2, aged 54, of coronary occlusion.

**Florence Gilman** ✠ Poughkeepsie, N. Y.; Tufts College Medical School, Boston, 1902; member of the Massachusetts Medical Society; at various times affiliated with Smith College, Northampton, Mass., Vassar College, Poughkeepsie, and Radcliffe College, Cambridge, Mass.; died in Meredith, N. H., July 31, aged 69, of coronary occlusion.

**Ralph Warren Goss,** Litchfield, Me.; Medical School of Maine, Portland, 1904; served as a member of the school board; died July 16, aged 68, of mesenteric thrombosis.

**Henry Matthew Grady,** Dedham, Mass.; Harvard Medical School, Boston, 1905; member of the American Medical Association; for many years physician for the welfare board; died July 30, aged 72, of cirrhosis of the liver.

**James Graybeal,** Chicago; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1907; member of the American Medical Association; formerly on the staff of the Englewood Hospital; died July 23, aged 73, of cerebral thrombosis and carcinoma of the prostate.

**Luther Hays,** Cullman, Ala.; Chattanooga (Tenn.) Medical College, 1900; also a graduate in pharmacy; member of the American Medical Association; veteran of the Spanish-American War; on the staff of Cullman Hospital; died July 7, aged 76, of carcinoma of the colon.

**Robert Reeves Hays** ✠ Akron, Ohio; Jefferson Medical College of Philadelphia, 1922; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychiatric Association; at one time affiliated with the Pennhurst State Hospital in Pennhurst, Pa., Blair County Hospital for Mental Diseases in Holidaysburg, Pa., and the Danville (Pa.) State Hospital; served on the staff of St. Thomas Hospital; died in Cleveland August 21, aged 48, of coronary occlusion.

**Thomas Francis Hennessey** ✠ Swampscott, Mass.; Tufts College Medical School, Boston, 1911; at one time practiced in Lynn, where he was for many years affiliated with the Lynn Isolation and Union hospitals; examiner of the draft during World War I; died July 21, aged 60, of coronary thrombosis.

**Paul Stanley Hill,** Saco, Maine; George Washington University School of Medicine, Washington, D. C., 1906; member of the American Medical Association; consultant at the Webber Hospital and co-owner of the Trull Hospital in Biddeford; died at his summer home in Biddeford Pool, July 26, aged 66, of coronary thrombosis.

**Harry Conrad Himmelman,** Chicago; Chicago College of Medicine and Surgery, 1912; on the staff of the Lutheran Deaconess Hospital, where he died July 20, aged 61, of coronary thrombosis.

**Farish Clay Holden,** Atlanta, Ga.; University of Georgia School of Medicine, Augusta, 1928; member of the American Medical Association; served as a member of the state board of medical examiners; medical consultant for the Veterans Administration; first lieutenant, medical reserve corps, U. S. Army, not on active duty; on the staffs of the Crawford W. Long and the Georgia Baptist hospitals; died in the Veterans Administration Hospital July 15, aged 47, of circulatory failure and chronic cholecystitis.

**Stanley Hall Holland** ✠ McKeesport, Pa.; College of Physicians and Surgeons, Baltimore, 1914; president of the McKeesport Academy of Medicine; affiliated with the staff of the McKeesport Hospital, where he died July 22, aged 59, of coronary occlusion.

**Alf Justin Holm** ✠ Chicago; Jefferson Medical College of Philadelphia, 1924; specialist certified by the American Board of Urology; fellow of the American College of Surgeons; served during World War II; clinical instructor in urology, department of surgery, University of Illinois College of Medicine; affiliated with the Alexian Brothers Hospital and the Ravenswood Hospital, where he died July 31, aged 49, of coronary thrombosis.

**Lewis Wade Hood,** Biloxi, Miss.; Mississippi Medical College, Meriden, 1911; past president of the school board; also a druggist; died July 24, aged 63, of heart disease.

**Claude Gibson Hooten,** Lynchburg, Va.; Bennett Medical College, Chicago, 1915; member of the American Medical Association; served during World War I; for many years medical examiner for the Norfolk and Western Railway; died in the Virginia Baptist Hospital July 25, aged 56, of heart disease.

**Edward T. Hornback** ✠ Hannibal, Mo.; Missouri Medical College, St. Louis, 1891; specialist certified by the American Board of Ophthalmology; on the staffs of St. Elizabeth's Hospital and the Levering Hospital, where he died July 15, aged 83, of coronary thrombosis.

**Edmund Newell Huff** ✠ South Pasadena, Calif.; Hahnemann Medical College and Hospital of Philadelphia, 1900; past president of the Bergen County (N. J.) Medical Society; at one time practiced in Englewood, N. J., where he was affiliated with the Englewood Hospital; at one time on the staff of the Holy Name Hospital at Teaneck, N. J.; on the staff of the Huntington Memorial Hospital in Pasadena; died July 3, aged 68, of aortic aneurysm and chronic hypertension.

**Charles Henry Ingram,** Fresno, Calif.; Cooper Medical College, San Francisco, 1903; member of the American Medical Association; on the staffs of St. Agnes Hospital and the Fresno Community Hospital, where he died July 28, aged 72, of cerebral thrombosis and cerebral hemorrhage.

**Henry Janoff** ✠ Trenton, N. J.; Temple University School of Medicine, Philadelphia, 1934; affiliated with St. Francis Hospital; died in the F. W. Donnelly Memorial Hospital July 11, aged 39, of pulmonary tuberculosis.

**Francis Arthur Jones** ✠ Lansing, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1903; fellow of the American College of Surgeons; on the staffs of Sparrow Hospital and St. Lawrence Hospital, where he died July 5, aged 73, of cerebral hemorrhage.

**Henry Nathan Kehres** ✠ Bryn Mawr, Pa.; Jefferson Medical College of Philadelphia, 1932; served overseas during World War I; on the staff of Bryn Mawr Hospital, where he died July 17, aged 49, of coronary occlusion.

**John Leo Kelliher,** Detroit; Chicago College of Medicine and Surgery, 1912; served in France during World War I; associated with the judiciary board of the Veterans Administration; served on the staff of the Veterans Hospital in Dearborn, Mich.; died in the Charles Godwin Jennings Hospital July 14, aged 60; of peritonitis following rupture of a diverticulum of the colon.

**Raymond Alexander Kinloch** ✠ Springfield, Mass.; University of Vermont College of Medicine, Burlington, 1903; member of the New England Obstetrical and Gynecological Society; on the staffs of the Wesson Memorial and Wesson Maternity hospitals; died July 5, aged 72, of heart disease.

**Allan Oscar Kisner,** Bethlehem, Pa.; College of Physicians and Surgeons, Baltimore, 1896; on the auxiliary staff of St. Luke's Hospital; died July 5, aged 82, of arteriosclerosis and bronchopneumonia.

**Claude Ross Laird** ✠ Ingleside, Neb.; Creighton University School of Medicine, Omaha, 1913; member of the American Psychiatric Association; served during World War I; for many years on the staff of the Hastings State Hospital; died in the Soldiers' and Sailors' Home in Grand Island, July 5, aged 66, of uremia and heart disease.

**Edward Nathaniel Lindquist** ✠ Culver City, Calif.; College of Medical Evangelists, Los Angeles, 1933; diplomate of the National Board of Medical Examiners; co-owner of the Community Hospital; died July 5, aged 42, in an airplane accident.

**Thomas Russell Littlejohn,** Sumter, S. C.; Medical College of South Carolina, Charleston, 1910; member of the American Medical Association; president of the Sumter County Medical Society; served during World War I; on the staff of the Tuomey Hospital, where he died July 26, aged 58, of cerebral hemorrhage.

**Thomas E. Livingston,** Portales, N. Mex.; College of Physicians and Surgeons, Keokuk, Iowa, 1887; died July 4, aged 86, of cerebral hemorrhage.

**Herman Meyer Lynch** ✠ West Bend, Wis.; Northwestern University Medical School, Chicago, 1908; health officer; served during World War I; member of the county selective service board during World War II; on the courtesy staff at St. Joseph's Hospital in Milwaukee and the regular staff at St. Joseph's Hospital in West Bend, where he died July 8, aged 63, of aneurysm and rupture of the aorta.

**Gustavus T. Lyon,** Roswell, Ga.; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1898; member of the American Medical Association; formerly a member of the state board of medical examiners; on the staff of the Crawford W. Long Memorial Hospital in Atlanta; died July 1, aged 75, of arteriosclerotic heart disease and nephritis.

**John J. McGarrell,** Baltimore; University of Maryland School of Medicine, Baltimore, 1908; died May 12, aged 64, of cerebral hemorrhage and hypertension.

**Edward Louis Miller,** Picher, Okla.; University Medical College of Kansas City, Mo., 1911; served during World War I; affiliated with the Picher Hospital; died July 18, aged 62, of angina pectoris.

**Albert Crombie Nixon** ✠ Los Angeles; Western University Faculty of Medicine, London, Ontario, Canada, 1914; on the staff of the Children's Hospital; died June 15, aged 59, of cerebral hemorrhage and hypertension.

**Joseph Tilford Scott** ✠ New Orleans; Medical Department of Tulane University of Louisiana, New Orleans, 1894; for many years affiliated with the U. S. Public Health Service; on the staffs of the Mercy Hospital and the Touro Infirmary; died July 5, aged 77, of coronary occlusion.

**Charles E. Sharp,** Elgin, Ill.; Chicago Homeopathic Medical College, 1895; Harvey Medical College, Chicago, 1900; died in the Sherman Hospital July 29, aged 86, of carcinoma of the stomach.

**Wilbur S. Slaughter,** Jonestown, Miss.; Memphis (Tenn.) Hospital Medical College, 1904; member of the American Medical Association; died July 14, aged 66, of heart disease.

**Jane Gray Stone,** Boston; Tufts College Medical School, Boston, 1911; died in the Massachusetts General Hospital May 6, aged 73, of pulmonary embolism.

**Elma Janes Townsend,** Madison, Wis.; Woman's Medical College of Baltimore, 1899; died in Maywood, Ill., July 2, aged 81, of coronary heart disease.

**Harvey Clinton Upchurch,** Dover, N. J.; College of Physicians and Surgeons, medical department of Columbia College, New York, 1893; died in the General Hospital July 21, aged 77, of coronary occlusion and hypertension.

**Walter Edward Zielinski,** Buffalo; University of Buffalo School of Medicine, 1917; member of the American Medical Association; served during World War I; bacteriologist for the city health department; died June 14, aged 57, of aortic insufficiency.

# Foreign Letters

## LONDON

*(From Our Regular Correspondent)*

Sept. 20, 1947.

### Vitamin D in Cutaneous Tuberculosis

In the section of dermatology Dr. J. Charpy (France) gave the results of vitamin D treatment in cutaneous tuberculosis; he introduced this treatment seven years ago. He now gives an adult 15 mg. of vitamin D in alcoholic solution twice a week for four weeks. He follows this with the same dose weekly for periods ranging from two months to two years. This treatment should be accompanied by a diet containing 1½ pints (670 cc.) of milk a day, with plenty of meat, fruit and vegetables. Fats should be taken sparingly and the salt intake much reduced, being omitted completely three days a week. The patient should take no alcohol or whole meal bread and should live in the open air. The good effects of treatment should be evident on the fifteenth day. If there was not improvement by then, failure of absorption must be suspected, or failure of tissue permeability, because of too much salt in the tissues. In successful cases there was no doubt about clinical cure; anatomic cure was more doubtful. If the treatment was pushed toxic symptoms were produced, which might culminate in acute nephritis.

Dr. G. B. Dowling (London) described his results from this treatment regimen, which he had adopted before he knew of Charpy's work. He gave doses of 150,000 units of vitamin D a day. He treated 39 patients to the end of 1945. Of these, 32 have been fully assessed; 18 are free from lupus and 9 improved, while 5 show no change. Since March 1946 he has treated 33 cases of cutaneous tuberculosis in adults and 11 in children. The adults had the disease an average of twenty years. Twenty-eight patients were discharged as free from lupus, but of these ten showed relapses, which responded to further treatment. In the early weeks of treatment the adult patients became worse and then began to improve. In one or two cases treatment with calciferol was followed by activation of a tuberculous focus in the lung. Dr. Dowling noted that Charpy reported nearly 100 per cent successes. His own results were not equal to this but were striking. On the other hand, others reported poor results, and it was hard to account for the great discrepancies.

### Penicillin

At the opening session Sir Archibald Fleming, the discoverer of penicillin, discussed this substance. It was the first successful antibiotic and set a high standard which no other antibiotic had yet reached. He discovered it by accident in 1928, while studying the staphylococcus. He forgot to put the lid on one culture plate, which became contaminated by an air-borne mold. Until recently all the penicillin in the world was made from the pure cultures grown from this contaminant. Following the observation that the mold produced lysis of the staphylococci growing near it, experiment showed that it had a selective action on some bacteria. When the mold was grown in a fluid medium, the fluid underneath contained a differential antiseptic, which was named penicillin. Other molds tested did not have this property. It was found that solutions of penicillin would diffuse through a much greater thickness of agar than could the old fashioned antiseptics and, in contrast with all other antiseptics then known, would kill staphylococci without harming leukocytes. In those early days penicillin was extremely impure—the best batches had a potency of only 1.5 units per cubic centimeter. Research in the United States has produced strains with a far greater yield.

Fleming has urged that penicillin be given only when the infecting organism is sensitive to it. The main objection to oil and beeswax mixtures—that they solidify on cooling—has been overcome. But prolonged action can equally well be obtained by injecting large doses of an aqueous solution. The most dramatic success of penicillin has been against gonorrhea. It is the only drug that allows a patient to have an attack twice a week! Indiscriminate use of penicillin is to be deprecated, because it is possible, though not easy, to render a sensitive organism resistant. The chairman, Lord Moran, said that as regards syphilis it is not known what the remote results of treatment will be.

Professor R. V. Christie submittd a report on the results of treatment with penicillin in 269 cases of infective endocarditis at the fourteen centers set up by the Medical Research Council. A dosage of 500,000 units a day was the most successful. It was a mystery why some patients did not respond though their infecting organism was no less sensitive than that of others who recovered. If a patient relapsed after one course he was unlikely to respond to a second. Most relapses occurred within twenty days but might arise after a year of health. Foci of infection should always be attended to. After a follow-up of at least a year Professor Christie had determined that in 95 per cent of the cases the infection could be controlled, but 39 per cent of the patients would die later. Heart failure was the major cause of death, accounting for 56 per cent of the fatalities, uremia for 6 per cent, emboli for 11 per cent, hemorrhage for 8 per cent and uncertain causes for 19 per cent. The risk of complications was more serious than the risk of not responding to penicillin therapy. The most significant points in prognosis were the degree of heart failure and the state of nutrition. With severe cardiac failure the outlook was practically hopeless, and the death rate among emaciated patients was 87.5 per cent. A sufficient dietary of protein was therefore essential.

## PARIS

*(From Our Regular Correspondent)*

Sept. 5, 1947.

### Vitamin $D_2$ in the Treatment of Lupus Vulgaris

Vitamin $D_2$ in an alcoholic solution, given per os, is claimed to cure completely and definitely tuberculosis of the skin. As stated by Professor Robert Debré at the scientific assembly of the Centennial Celebration of the American Medical Association, signs of intolerance through too strong doses have been seen. At one of the recent meetings of the National Academy of Medicine J. Charpy (Dijon) has explained the results of his research on the process of action of vitamin $D_2$; he thinks that a certain amount of vitamin $D_2$ increases the activity of intestinal phosphatases and that with stronger doses there occurred, moreover, activation of other phosphatases in the kidneys and in the bones, which produced intoxication.

He relies on two groups of facts:

1. Magnesium, an activator of alkaline phosphatases, supplements the therapeutic effect of vitamin $D_2$ without diminishing the margin of tolerance, if administered orally in the form of magnesium chloride (1½ Gm.) a little while before the vitamin $D_2$ is taken. However, intravenous magnesium sulfate (1½ Gm.) increases the effect of vitamin $D_2$ but diminishes the margin of tolerance. Why this difference of action? In the case of oral magnesium chloride the amount of magnesium in the blood does not sensibly vary and only the intestinal phosphatases are activated; by the intravenous administration of magnesium sulfate the renal and osseous phosphatases are stimulated at the same time.

2. Cysteine is a strong inhibitor of the phosphatasic action; Charpy and P. Pichat have observed that the daily injection of 0.001 Gm. of cysteine suppresses the therapeutic effect of a large dose of vitamin $D_2$ given orally in an alcoholic solution and, at the same time, the accidents due to intolerance. Therapeutic activity and intoxication are, then, two effects with a single cause. As a consequence, Charpy thinks that vitamin

$D_2$ reacts on the lupus not by itself but through products of the hydrolysis of the intestinal phosphastase transferred to skin by means of the circulation. The author has also reported a clinical experimental observation, in which an open tuberculous lesion, rich in Koch's bacilli, has been sterilized through a complex treatment consisting of (*a*) oral magnesium chloride, vitamins $D_2$, $B_1$, $B_2$ and C (ascorbic acid), phosphoric acid and nicotinamide and (*b*) direct contact of muscular adenylic acid.

### New Books on Pulmonary Tuberculosis

Two remarkable books by G. Canetti, laboratory chief at the Cochin Hospital and assistant at the Pasteur Institute, have been published by Ernest Flammarion, 20 Rue du Vaugirard, Paris, (under the guidance of Professor Pasteur Vallery-Radot and Professor Agrégé J. Hamburger) in the collection of the Pasteur Institute.

"Koch's Bacillus in the Tuberculous Lesion of the Lung" sets forth the anatomicohistobacteriologic and clinical research on 1,500 cases for seven years. The author has examined the abundance and the rarity of the tubercle bacillus according to the various stages of tuberculosis. He has found in histologic sections an average of 13 bacilli in one hundred fields in fibrinous alveolitis; only 6 in one hundred fields in solid caseation, but up to 150,000 in one hundred fields of caseation in process of softening. In the cavities (in the internal necrotic zone) there is an average of 8,000 in one hundred fields. The causes of these variations are unknown. Canetti thinks that they are probably ascribable to changes in the local conditions, which create a medium sometimes favorable, sometimes unfavorable to bacillary development.

"Tuberculous Allergy in Man" sets forth the results of research on 4,500 cases. Against the broader definition of allergy by Rist and others, the author adopts a restricted definition of allergy as a hypersensitivity which appears in the organism when first infected. He studies it in latent tuberculosis, in osteoarticular and cutaneous tuberculosis. He also studies the mechanism of allergy, which, according to him, does not yield any information which could be of profit for the diagnosis or the prognosis; its value is questionable. It is at the same time useful and noxious on account of the strong reaction which has an influence on the trend of phthisis. The primary role, as regards protection, belongs, according to the author, to the natural resistance of the organism. The evolvement of a precise test rendering possible the detection of subjects resistant to tuberculosis is of primary importance. The author believes it possible that subjects whose tuberculin reactions are negative after having been positive are endowed with a strong natural power of resistance contributing to the rapid sterilization of latent lesions.

### Adnexitis

On the agenda was adnexitis. J. Dalsace emphasized the role of hysterosalpingography and of insufflations in the diagnosis and treatment of salpingitis. He insisted on the association of those two processes with conservative surgery of the oviducts. Y. Canel and P. Neumand demonstrated, on observation of thousands of cases, that 85 per cent of patients respond successfully to hydromineral treatment. R. Bougarel and H. Ezes reported 8 cases of salpingitis due to intestinal parasitism. Arnaldo de Moraes and João Bruno Lobo (Rio de Janeiro, Brazil) reported 68 cases of adnexitis treated with four consecutive applications (50 r each) of roentgen therapy. In 42 cases (64 per cent) they obtained extremely favorable results, in 16 (24 per cent) indifferent ones; 8 cases (12 per cent) have been failures. J. Delmas and Y. Andreani used with success local penicillin therapy associated with a *véhicule retard* and added vitamin H (biotin), which renders it effective against Escherichia coli. In a series of abscesses of the breast, they obtained spectacular results by the local use of penicillin and avoided surgical operation. The same authors reported 90 patients (50 post abortum and 40 post partum) prophylactically treated with great success by direct introduction into the uterus after obstetric proceedings (such as curettage) of an average of 5 Gm. (ten tablets) of sulfanilamide. The Congress has expressed several wishes, which have been forwarded to the public authorities; (1) that the Social Security Organization recognize adnexitis as a disease of long duration; (2) the creation by the Faculty of Medicine of a Gynecologic Certificate for the specialists of this branch, and (3) the inclusion of a sperm examination among other laboratory tests in the prenuptial examination because of the increase of male sterility (35 per cent).

### Eleventh Congress of French Gynecologic Society

This Congress, at which twelve nations were represented, took place at Châtelguyon, May 31-June 3, 1947. The opening speech was delivered by the honorary president, Dr. J. C. Rubin of New York, representing the American Gynecological Society. He said among other things that: "Medicine is democracy in action; it knows of no barrier, no secret formula; the same biologic laws apply to kings as to ordinary citizens, to whites and Negroes, to aristocrats and laborers. True Medicine knows of no hatred. Nature in its different kingdoms offers a striking evidence of unity in diversity. Science, Democracy and Medicine are an absolute whole."

## BUENOS AIRES

*(From Our Regular Correspondent)*

Sept. 10, 1947.

### Transthoracic Injection of Streptomycin

According to a communication to the National Academy of Medicine, Drs. M. R. Castex, E. L. Capdehourat and C. Rechniewski injected streptomycin directly into the thorax in 2 cases of chronic pulmonary suppuration (a more precise characterization of the disease is not given) in which every other therapeutic procedure, including nebulization of sulfonamide drugs and penicillin, had been without success. They chose the transthoracic route to administer the small quantity of streptomycin available.

The sputum of the first patient showed, before this treatment, a flora particularly rich in gram-negative organisms (Klebsiella pneumoniae and coliform bacilli). After the transthoracic injections of streptomycin the bacterial flora diminished in quantity and quality. Both the aforementioned bacilli disappeared after the fifth injection, but after the eighth injection some gram-negative organisms reappeared (although in a small number) and did not disappear again until the end of the treatment (acquired resistance?). The presence of an effective amount of streptomycin in the sputum could be proved. The quantity of sputum diminished from 85 cc. per day to 25 cc. after the sixth injection, coincident with the disappearance of the gram-negative bacilli, but later on increased again.

In the second case also previous intrapulmonary injections (see THE JOURNAL, Oct. 5, 1946, p. 303) of sulfonamide compounds, neoarsphenamine and other agents—two hundred injections in all—had had a transitory effect (if any). With streptomycin therapy the number of organisms diminished considerably following the third injection and remained so until the end of treatment. The gram-negative bacilli disappeared at the same time but reappeared in a much lower concentration after the seventh injection and remained so until the treatment was terminated.

From their observations the authors conclude that the action of streptomycin is only transitory and bacteriostatic but not bactericidal. After the treatment had been terminated, the bacterial flora reappeared. The pyogenic process of the lung had not been cured, although the streptomycin had been diffused

efficiently in the morbid focus. The injection of 1 Gm. of the drug is adequate for twenty-four hours, while for other routes of injection greater amounts are necessary. This circumstance seems of importance also with respect to disagreeable side reactions provoked by greater quantities of the substance. The frequency of the injections depends on the clinical and bacteriologic data obtained. According to the observations in the 2 cases mentioned, one transthoracic injection per day is sufficient (contrary to the need for more intramuscular and intravenous applications). The transthoracic injections should be continued after the gram-negative bacteria have disappeared, to make the cure certain. If during treatment the gram-negative bacteria reappear, the dose of streptomycin should be increased, because the reappearance indicates a certain degree of resistance to the drug. In both the observed cases the application of streptomycin could not be continued according to these rules due to the lack of the drug.

### Intra-Articular Administration of Penicillin

Occasionally cases of acute articular processes are seen which affect only one or two articulations but these with much intensity (and not many joints in a more superficial degree). It is the form which Chauffard designated rheumatic pseudophlegmon. According to a communication of Dr. Guido Costa Bertani to the Society of Internal Medicine of Buenos Aires it is characteristic for this condition to be resistant to any usual form of treatment. A quick therapeutic success, however, is necessary to overcome the great danger of cartilaginous destruction. Sulfonamide compounds are without effect; a gold preparation is somewhat better but not always possible to administer, due to the sensitivity of many patients to this substance, and sometimes dangerous. Penicillin given intramuscularly or intravenously also has little effect (if any). Therefore Dr. Costa Bertani tried the intra-articular administration of penicillin directly into the affected joint. After obtaining a good result in the first patient (who was absolutely resistant to any other treatment) with only two intra-articular injections, this method has been tried in more cases (4 of which are described in extenso) with complete and immediate success. The dosage of penicillin varies between 5,000 and 20,000 Oxford units (10,000 per cubic centimeter). It is supposed that the rapid improvement is exclusively due to the intra-articular administration of penicillin.

### Cardiology as a Specialty

The Faculty of Medicine of Buenos Aires has created the title of Cardiologist. To be qualified as such the candidates must be an M.D. at least two years and attend a special instruction course of two years' duration, practical as well as theoretic, which includes pathologic anatomy, physiopathology, semiology, pharmacology and therapeutics, radiology, electrocardiology and cardiologic clinic. The number of participants is limited; they pay each year 100 pesos for matriculation and 720 pesos for the training. Seventy per cent of this amount is distributed among the teachers, who must be recognized specialists elected by the director of the course, who himself must be a professor of the faculty and is appointed by a special commission of the same. Twenty per cent is for instruction expenses and the last 10 per cent for administrative expenses. After one year the candidate has to pass an examination of "sufficiency," to which he is admitted only when he has attended at least 80 per cent of the lectures and has satisfactorily completed all the practical work. Without having passed the examination at the end of the first year he cannot register for the second year.

### Sterility Due to Absence of Germinal Epithelium

Drs. E. B. del Castillo, F. A. de la Balze and A. Trabucco observed 5 cases of a new syndrome, the principal characteristics of which are sterility and small testicles in men who are otherwise normal. Biopsies of the testicles proved the complete absence of the germinal epithelium while Leydig's cells were normal; the tubules likewise had walls of normal structure and contained apparently normal Sertoli's cells. To explain the absence of the germinal epithelium the authors suppose—as a hypothesis—that the primary gonocyte did not penetrate in the primary testicle. The follicle-stimulating hormone in the urine was of normal quantity, the 17-ketosteroids somewhat diminished. They suppose that Sertoli's cells are the source of a hormone which is similar to estrogen which controls the production of the follicle-stimulating hormone of the hypophysis.

### Ulcer of Cornea Caused by Thiocyanate

In 1944 Drs. Juan M. González and José Dorning Muñoz of the Spanish Hospital at Rosario reported 10 cases of ocular complications during the treatment of hypertension with potassium thiocyanate (of which 1 was ulcer of the cornea). They therefore advised an average dose of no more than 0.3 Gm. (0.2 to 0.4) per day, with which they had never observed toxic manifestations of importance, especially when given intermittently (during four or five days, then interrupted for two or three days). But in spite of these precautions 3 more cases of corneal ulcer have been observed by the same authors in the last two years. They admit that these observations are rather infrequent and that they have not been able to establish exactly the relation of cause and effect between the medicament and the lesion. However, it seems notable that the ocular alterations appeared simultaneously with the administration of the thiocyanate and disappeared when this medicament had been discontinued. The character of the lesions was benign with restitution ad integrum in a few days.

### Prominent Visitors at Buenos Aires

It seems to us a good symptom of the intensified scientific interchange that—apart from eminent specialists who will be mentioned under "Brief Items" and who are particularly Americans—some prominent physicians have visited the Argentine during the last weeks. The first of them has been Dr. Morris Fishbein, who in his very active way visited in a short time all the important scientific institutions of Buenos Aires. He has been received by all the Argentine leaders of medicine, addressed the Academy of Medicine, speaking on recent progress in medicine, has been made a corresponding member of the Argentine Medical Association and made, indeed, a great lot of new and sincere friends.

Prof. Dr. de Gennes of the Faculty of Medicine of Paris read several papers on endocrine questions, particularly on pellets of hormones and on the endocrine treatment of hypertrophy of the prostate.

Professor Louis Michaud, director of the medical clinic of the Faculty of Lausanne (Switzerland) read papers on the respiratory function, the metabolism of iron, hereditary problems in neurology and some kidney problems, describing the research by his clinic during the last years. He also became a corresponding member of the Argentine Medical Association.

Dr. Georges Duhamel, writer, who is also a physician, addressed the National Academy of Medicine, speaking of the merits of the French investigator Charles Nicolle. He has been made an honorary member of the academy.

### Brief Items

Prof. Dr. Domingo Brachetto Brian has been appointed by the government new director of the Instituto de Medicina Experimental, replacing Dr. Angel H. Roffo, who had to retire some months ago and died on July 24, at the age of 65. Dr. Brachetto Brian, who is a pathologist, studied in France with Roussy, Pierre Marie and several well known surgeons and also in the Curie Institute. He is professor extraordinary of the Faculty of Medicine of Buenos Aires and since 1936 has been director of the department of pathologic anatomy of the Hospital Ramos Mejía in Buenos Aires.

# Correspondence

## COMPLEX SIMPLE FRACTURE

*To the Editor:*—Realizing that the term "simple fracture" as generally defined is thoroughly inadequate to describe the trauma received in many so-called simple fractures, I have added a new definition to the simple and compound fracture nomenclature, i. e., "complex simple fracture" (Key, J. A., and Conwell, H. E.: The Management of Fractures, Dislocations and Sprains, ed. 4, St. Louis, C. V. Mosby Company, 1946, pp. 41-43).

A complex simple fracture is a fracture which is not compound but which has received severe trauma to either or all of the surrounding soft structures, i. e., skin, muscles, blood vessels and nerves. The bony fragments usually are displaced to a marked degree.

"Complex," as defined by "Webster's New International Dictionary," unabridged, is as follows: (1) an assemblage of related things; (2) a whole made up of complicated or interrelated parts.

The complex simple fracture should be further described as to the type of bony injury, for example: complex simple fracture (transverse, comminuted, spiral or oblique, as the case may be).

Through personal contacts and correspondence with the personnel of the three National Fracture Committees (American Medical Association, American College of Surgeons and American Academy of Orthopaedic Surgeons) with reference to their opinions and the necessity for such new fracture term or definition, there was unanimous agreement that such a definition of complex simple fracture was a necessary one and should be generally accepted and used in its broad meaning.

I make an appeal that this new fracture definition or its relative equivalent be used by the members of the medical profession. Besides expressing more adequately the pathologic process in such type fracture it will mean improved records for the hospitals and convey a better description of the fracture to the insurance companies, compensation boards and other related agencies, thereby being of much help to the patient, the physician and every one concerned.

I will appreciate any opinion or suggestions relative to the foregoing.

H. EARLE CONWELL, M.D., Birmingham, Ala.

## ALLERGIC REACTIONS TO TYPHOID (T. A. B.) VACCINE?

*To the Editor:*—During the past months I have been variously interrogated whether I had any knowledge of allergic reactions after typhoid or T. A. B. vaccination. So far I have always given a negative answer. In numerous cases fainting was allegedly observed a few hours after the injections. In 1 case it was reported that a dangerous collapse had taken place.

When asked why an allergic case should be suggested, physicians based their diagnosis on Theodore J. Curphey's paper "Fatal Allergic Reaction Due to Influenza Vaccine" (THE JOURNAL, April 12, p. 1062). In that report a previous paper of V. E. Roth is cited: "Thus Roth reported 9 cases of allergic reactions to typhoid vaccines, in only 4 of which the patient gave a reliable history of allergy to egg protein." As typhoid vaccine is not prepared with any egg products I supposed a misprint. Roth's paper in the *United States Bulletin of the Army Medical Department* 1945 was inaccessible to me, so I looked up its abstract in THE JOURNAL (July 21, 1945, p. 904), where I gathered that the reported 9 cases of allergic reaction were derived not from typhoid but from typhus vaccine. This proves that the fears of an alleged influence of typhoid vaccine of allergic reaction are utterly baseless.

M. J. GUTMANN, M.D., Jerusalem, Palestine.

## THE EPIDEMIOLOGY OF POLIOMYELITIS

*To the Editor:*—Sabin asks in his article on "The Epidemiology of Poliomyelitis" (THE JOURNAL, June 28) Why did paralytic poliomyelitis become an epidemic disease only a little more than fifty years ago, and as such why does it seem to be affecting more and more the countries in which sanitation and hygiene, along with the general standard of living, are presumably making the greatest advances, while other large parts of the world, regardless of latitude, are still relatively unaffected?

My answer:

Let us take the hypothesis that a B hypovitaminosis is a disposing factor for poliomyelitic paralysis (see C. Braendli-Wyss: Propositions for Prophylaxes of the Poliomyelitic Paralysis, *Schweiz. med. Wchnschr.* **2**:40, 1945). The general B hypovitaminosis induced by the milling of fine flour and other changes in nutritional habits is followed in time by the appearance of the first poliomyelitic paralysis epidemic. Apart from that the countries with the best developed hygienic conditions are those with pronounced B hypovitaminosis. I am sure this is only one part of the problem, but I think it would be of general interest to discuss this in THE JOURNAL.

In any case it would be worth while to carry through an experiment on a large scale with your incomparable possibilities in schools or other institutions in your country by additional vitamin B supply.

C. BRAENDLI-WYSS, M.D.
Burgdorf, Switzerland.

## IMMUNIZATION PROCEDURES IN PEDIATRICS

*To the Editor:*—In the discussion to the paper "Immunization Procedures in Pediatrics" given by J. J. Miller Jr. (THE JOURNAL, July 26), Dr. Thelander spoke about the variability of the capacity to be immunized as an important factor of vaccination. We have studied this variability by means of several thousand titrations of antibodies in vitro and in vivo and we have shown that the curve obtained by plotting logarithms of titer against incidence is a curve of normal distribution; this predisposition for immunity is hereditary and is different for different antigens in the same subject; i. e., a person who is prone to produce a good antibody response to one antigen does not show, on the average, a similar predisposition to produce other antibodies. Some exceptions to this rule are interesting only from a theoretical point of view (*Boll. Ist. Sieroter, Milanese* **24**:215, 1945, IV International Congress of Microbiology).

I have read with great interest the conclusions drawn by Dr. Miller and Dr. Thelander on the subject of immunization in older ages. In several Italian towns we have used an oral method of restoration of diphtheria immunity in adults and have obtained with the vaccine we have prepared good results: one 100 Lf tablet dissolved in the mouth daily for seven days was sufficient in more than 90 per cent of the adults to provoke a striking increase of antitoxin in the blood serum (in many cases from $< 0.02$ unit to more than 2 units) (*Riv. Ist. Sieroter. Italiano* **22**:49, 1947).

To avoid confusion in the American readers of European literature, I would like to point out also that the standardization of H. pertussis vaccines using the European standards of turbidity (Wellcome opacimeter, etc.) does not correspond to the American one. European vaccines have a concentration of bacteria approximately three times as strong as the American vaccines having the same labeled strength.

E. CARLINFANTI, Naples.
Istituto Sieroterapico Italiano.

# Bureau of Legal Medicine and Legislation

## MEDICOLEGAL ABSTRACTS

**Workman's Compensation Act: Release Based on Untrue Statements of Physician May Be Set Aside.**—The plaintiff filed an action to set aside a release made in a compromise settlement of an industrial accident injury. From a judgment for the plaintiff the defendant appealed to the Court of Civil Appeal of Texas.

The plaintiff suffered an injury in the course of her employment when some steel dust and shavings from a machine she was operating were blown into her eyes. After being under the care of a physician selected by the employer for some five weeks, during which time she did not work because of her eye condition and headaches, the defendant's claim agent called on her, said he had been informed that she had been dismissed by the physician and wanted to discuss a settlement of her claim. The plaintiff denied the dismissal, answering that she had another appointment the following Monday, and the claim agent left saying he would see the physician. A few days later he came back with the same information. The plaintiff again questioned the statement, whereupon the claim agent asked her to call the physician on the phone which she did. She said she recognized the doctor's voice; he told her that she should have been already advised about a dismissal, then dismissed her, saying that her eyes were all right and "It would be all right for me to settle." Accordingly she entered into a compromise settlement and signed the release in question. It subsequently developed, however, that the plaintiff was slowly losing the use of her eyes due to deterioration of the optic nerve; that there were scratches on the eyeball surface; that both eyes were infected, the infection going down to the corneal margin; that the plaintiff had photophobia, with evidence of injury to the cornea of the eye by particles of steel; that the plaintiff's trouble was slow deterioration of the optic nerve and inability of the eyes to fuse images; that the defect was in the nerve and could not be cured by glasses; and that the injury sustained at the plant reasonably caused the condition of the plaintiff's eyes.

This action, said the Court of Appeals, is based on the well settled equity doctrine that representations of an existing fact or condition by a releasee's doctor, relied on by the releasor, are sufficient grounds for avoidance if the representations are proved to be untrue in fact. The defendant, however, contended that this principle was not applicable because the evidence showed that the plaintiff knew in her own mind at the time she signed the release that her eyes were not getting well. The court said, however, that "The fact that the releasor had doubts as to the correctness of the representations of the physician of the releasee regarding the extent of his injuries will not prevent the setting aside of the release, on the theory that in executing it the releasor acted on his own judgment, and not on that of the physician, if in fact the representation of the latter did in fact influence him in making the settlement." On a review of all the evidence, the court was of the opinion that the judgment in favor of the plaintiff setting aside the release should be affirmed.—*Associated Employers Lloyds v. Aiken, 201 S. W. (2d) 856 (Texas, 1947).*

**Railroad Hospital as Public Charity Exempt from Taxation**—Pulaski County, the City of Little Rock, the Little Rock Special School District and an individual property owner filed a petition with the Arkansas Public Service Commission to have the property of the defendant hospital association placed on the assessment roll for ad valorem taxes. The Public Service Commission made the order requested by the plaintiffs, which order was affirmed by the Pulaski Circuit Court, so the defendant appealed to the Supreme Court of Arkansas.

Article 16, section 5, of the Arkansas constitution says, in part, ". . . the following property shall be exempt from taxation: . . . buildings and grounds and materials used exclusively for public charity." And the defendant claims that its property is exempt under the aforequoted portion of the constitution.

Defendant is a benefit association organized under the laws of Missouri and composed of the employees of the Missouri Pacific Railroad Company and the Missouri Pacific Transportation Company. Defendant owns the hospital in Little Rock, and the employees of the railroad and transportation companies support the hospital by contributions from their wages and salaries each month and these employees have absolute and exclusive control over the hospital. The hospital is principally opened to retired employees of these companies and to members of their families, but, in addition, the hospital receives some people who become sick or are injured on the property of the railroad or transportation company. The hospital does not "go out and take in the public generally that might come in and ask for admission." The employee contributions are fixed by the board of trustees of the hospital, based on a scale depending on the amount of wages of each employee. The assessments are made to meet the requirements of the hospital and, in the event that the hospital accumulates a surplus, the assessments are reduced or temporarily suspended.

These facts, said the Supreme Court, show that the property is not used "exclusively for public charity." In a prior Arkansas case the Supreme Court held the following to be some of the essentials (existing in that case) necessary to allow exception of property "used exclusively for public charity": A. The institution was opened to any worthy sick person regardless of ability to pay. B. No funds were diverted from the institution and whatever profit was realized from those who paid went to the benefit of those who could not pay, to extend and enlarge the charity of the hospital. Neither of these two essentials, the court pointed out, is present in the case at bar. The defendant hospital is not open to "any worthy sick person"; it is open only to the Missouri Pacific employees, their families and persons who may become sick or injured on Missouri Pacific property. Furthermore, if the hospital accumulates a surplus it is returned to the members by reducing or temporily suspending assessments. In short, the proof shows that the hospital is not used "exclusively for public charity" and the use is the determining factor.

Continuing, the court said that a most enlightening case, construing the Arkansas constitutional provision as applied to a hospital operated for benefit of railway employees, is *St. Louis Southwestern Railway Company* v. *Yates*, 23 F. (2d) 283. In that case the United States Circuit Court of Appeals of the Eighth Circuit decided that a hospital in Texarkana, Ark., was not exempt from taxation. The court said "Funds to support the institution are to be obtained by assessments, based on a wage earning scale, collected monthly from the employees. There are other provisions which emphasize those above quoted or outlined but sufficient has been said to show the general plan of the trust to be that the use of the property is confined to the employees (and their dependents) of appellant and its affiliated lines. The public in general, nor any part thereof nor any indefinite class have any right to any use in this property and it is in no wise supported by any charitable gifts or donations, but only by the direct beneficiaries thereof and by contributions, in the form of loans, from the railways whose employees are protected. In short, it is merely the familiar plan of a hazardous business providing hospital and medical services for those engaged therein. It seems to us that this is clearly not a usage 'exclusively for public charity.' . . ."

The defendant relied most strongly on act 40 of 1931 as granting the exemption from taxation. This act provides: "All corporations or institutions heretofore or hereafter organized, created and operated as a hospital for the purpose of treating the members of said organization and others, not leased or otherwise used with a view of profit, are hereby declared to be institutions of public charity and shall be free from taxation." But the vice of the defendant's argument in reliance on this act, said the Supreme Court, lies in the unconstitutionality of the act as applied to the facts of this case. Article 16, section 5, of the constitution provides what property is exempt from taxation; article 16, section 6, provides: "All laws exempting property from taxation other than as provided in this constitution shall be void." When we held as we have above that the defendant's property was not "used exclusively for public charity," then article 16, section 6, of the constitution strikes down any legislative attempt to grant defendant any exemption

from taxation. We therefore conclude that act 40 of 1931 is unconstitutional in so far as it attempts to grant tax exemption to property not exempt under article 16, section 5, of the constitution and for that reason does not support the defendant in this case.

Finally, the defendant cited orders of the Pulaski County Court, made in 1925 and 1931, and an order of the Arkansas Tax Commission, made in 1929, each declaring defendant's property to be exempt from taxation and claimed that these orders rendered res judicata any and all questions as to taxability of defendant's property in the present proceedings. We hold, said the court, that a judgment rendered in one year, holding property to be exempt from taxes because "used exclusively for public charity," is not res judicata regarding the taxes of the property for a subsequent year. The great weight of authority is to the effect that an adjudication on liability for taxes of one year is no bar to an action for taxes for a subsequent year. We therefore hold that the defendant's plea of res judicata is without merit.

A dissenting opinion states, in part, "It will be observed that the exempting provisions of the constitution do not attempt to define 'public charity,' so as I view it, the present case presents this question: Can the legislature within reasonable limitations find and declare as the public policy of this state what constitutes public charity and what types of institutions shall be declared institutions of public charity? I think it has that power. Certainly, the legislature of this state has the power to, and does, declare the state's public policy and when, as here, it has by legislation declared the state's public policy to be that all corporations or institutions coming within the provisions of act 40, supra 'are hereby declared to be institutions of public charity and shall be free from taxation,' it was, it seems to me, acting within its powers and this court would not be warranted in striking down this legislation as being in contravention of the constitution."

The judgment of the circuit court holding the hospital association property to be taxable was affirmed.—*Missouri Pacific Hospital Association v. Pulaski County, 199 S. W. (2d) 329 (Ark., 1947).*

**Unauthorized Autopsy—Mistake in Identity of Corpse.**—The plaintiff sued for damages alleged to have been sustained by virtue of the performance of an unauthorized autopsy on the body of her deceased husband. The defendants are the manager of health and charity and ex officio coroner and superintendent of the Denver General Hospital, the deputy coroner in charge of the morgue and the pathologist for the Denver General Hospital. From a judgment for the plaintiff, the defendants appealed to the Supreme Court of Colorado.

The plaintiff's husband and one William Lloyd were patients in the Denver General Hospital and occupied adjoining beds in the same room. Both men died on the same day, just five minutes apart. Pursuant to the rules and regulations of the hospital, the room nurse, who had been taking care of both patients, prepared death tags for them but "through mistake or inadvertence" she attached the tag prepared for Lloyd to the body of the plaintiff's husband. Following the deaths, the Lloyd family consented in writing to an autopsy on his body, but the plaintiff refused to consent to an autopsy on the body of her husband. Because of the mistake in the tags, however, the wrong body was delivered to the morgue and consequently the defendant Williams, pathologist at the hospital, with no knowledge of the circumstances, proceeded mistakenly to perform an autopsy on the body of the plaintiff's husband. The autopsy was performed in a proper and scientific manner.

The court first pointed out that the city itself was not liable. Municipal corporations, said the Supreme Court, exercise two classes of powers, "one . . . is of a public and general character, to be exercised in virtue of certain attributes of sovereignty delegated to it for the welfare and protection of its inhabitants; the other relates only to special or private corporate purposes, for the accomplishment of which it acts, not through its public officers as such, but through agents or servants employed by it. In the former case its functions are political and governmental, and no liability attaches to it, either for nonuser or misuser of power; while in the latter, it stands upon the same footing with a private corporation, and will be held to the same responsibility with a private corporation for injuries resulting from its negligence. . . . The authorities are practically agreed in placing certain general duties in the class that is governmental, and among those is the general duty of the preservation of the public health." Considering, continued the court, that the hospital, where the events upon which plaintiff relies occurred, was maintained and operated "for the purpose of preserving and maintaining the health of the people of the said City and County of Denver," we are pursuaded that the municipal entity was carrying on in its governmental, not its corporate, capacity, hence would not be liable.

Likewise, continued the court, those subjected to action here must stand absolved from liability. Schwalb, the manager, Economy, the deputy coroner, Williams, the pathologist, and the nurse who erred in attaching death tags, all were employees of the identical employer, the City and County at Denver. The basic error was that of the nurse, who was not made a party defendant. Defendants Schwalb and Economy had no part in what occurred, did not order or direct it, or even have knowledge thereof. Defendant Williams proceeded in accordance with information made manifest in apparent and usual course, and, so far as appears, without any wantonness, evil intent or wrongful purpose. In such circumstances, what he did was not actionable. The occurrences, clearly resulting from untoward happenings, were most unfortunate and regrettable. So far as revealed, however, all were the logical result of lack of care of the nurse, who was not made a party defendant. "The doctrine of respondeat superior applicable to the relation of master and servant does not apply to a public officer so as to render him responsible for the acts or omissions of subordinates whether appointed by him or not, unless he, having the power of selection, has failed to use ordinary care therein, or unless he has been negligent in supervising the acts of such subordinates, or has directed or authorized the wrong." In order for these exceptions to the rule to have consideration, however, the court concluded, they must be alleged in the complaint, which was not done in this case. Accordingly the judgment in favor of the plaintiff was reversed.—*Schwalb v. Connely, 179 P. (2d) 667 (Colo., 1947).*

# Medical Examinations and Licensure

## COMING EXAMINATIONS AND MEETINGS

### BOARDS OF MEDICAL EXAMINERS
### BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Examinations of the boards of medical examiners and boards of examiners in the basic sciences were published in THE JOURNAL Oct. 18, page 452.

### NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: *Part III.* New Haven, Jan, 7-9; New York, Jan.; San Francisco, Dec. 16-18; Washington, Nov. 11-13. Exec. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia 2.

### EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF NEUROLOGICAL SURGERY: *Oral.* Chicago, May or June. Final date for filing application is Feb. 1. Sec., Dr. W. J. German, 310 Cedar St., New Haven, Conn.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Part I. Written.* Various Centers, Feb. 6. Final date for filing application is Nov. 1. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh 6.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Part I.* April-May. Applications are accepted for the next examination until Jan. 15, 1948. Sec., Dr. Francis M. McKeever, 1136 W. 6th St., Los Angeles 14.

AMERICAN BOARD OF PEDIATRICS: Dallas, Dec. 5-7. Philadelphia, Jan. 9-11. Sec., Dr. Lee F. Hill, 718 Royal Union Bldg., Des Moines 9.

AMERICAN BOARD OF PLASTIC SURGERY: Examinations are given in April and November of each year in the home town of applicants. Sec., Dr. Robert H. Ivy, 1930 Chestnut St., Philadelphia.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: *Oral.* May 1948. Final date for filing application is Feb. 15. Sec., Dr. F. J. Braceland, 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF RADIOLOGY: *Oral.* Chicago, June 1948. Final date for filing application is March 1. Sec., Dr. B. R. Kirklin, 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Written.* Various Centers, March. Final date for filing application is Dec. 1. Sec., Dr. J. S. Rodman, 225 S. 15th St., Philadelphia 2.

AMERICAN BOARD OF UROLOGY: Chicago, February. Final date for filing application is Nov. 1. Sec., Dr. Harry Culver, 1409 Willow St., Minneapolis 4.

# Current Medical Literature

## AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1937 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied with stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

### American Journal of Diseases of Children, Chicago

**74**:1-120 (July) 1947

Cerebral Damage in Infants and in Children: Observations on Its Causes and Possibilities of Its Prevention. H. K. Faber.—p. 1.
*Early Immunization Against Pertussis. J. M. Adams, A. C. Kimball and F. H. Adams.—p. 10.
Oral Administration of Penicillin in Pediatrics. H. A. Reisman, A. A. Goldfarb and Molly Molloy.—p. 19.
Syndromes of Kerosene Poisoning in Children. M. M. Steiner.—p. 32.
*Secondary Pancreatitis. P. V. Véghelyi.—p. 45.
Factors Influencing Retention of Nitrogen and Calcium in Period of Growth: VII. Effect of Methyl Testosterone. J. A. Johnston.—p. 52.
*Islet Cell Tumor of Pancreas in Newborn Infant (Nesidioblastoma). H. Sherman.—p. 58.
Diphtheria of Esophagus: Case Involving Stomach and Tongue. A. L. Hoyne.—p. 80.

**Immunization Against Pertussis.** — Adams and his co-workers studied a selected group of mothers and babies who were followed at approximately monthly intervals throughout the first year of the infant's life. Infants were given three inoculations consisting of phase I superconcentrate vaccine, 2.5 cc. (40 billion organisms per cubic centimeter) or a total dose of 100 billion organisms given at weekly or monthly intervals. The dosage schedule was 0.5 cc., 1 cc. and 1 cc. Mothers who were immunized during the last trimester of pregnancy were given three inoculations at two week intervals for a total of 100 billion organisms. With weekly inoculations good antibody titers could be demonstrated in over half of the infants by the age of 1 month to 6 weeks. Monthly inoculations gave a slower but more permanent rise. A combination of the two procedures might offer the best chance of early protection to the infant. Increased dietary protein did not enhance the infant's capacity to form antibodies. Specimens of cord blood from mothers immunized in the last trimester of pregnancy contained antibodies but in somewhat lower amounts than the mother's serum. This antibody titer is gradually lost by the infant during the first six months of life. One hundred and forty-two pairs of specimens of antepartum and cord blood from unimmunized mothers were tested. Hemophilus pertussis antibodies were absent in both specimens in 109 pairs. Hemophilus pertussis antibodies were present in colostrum but in lower titer than in the maternal or cord blood; their significance in the human being is probably negligible.

**Secondary Pancreatitis.**—Véghelyi reports 1 case of mild pancreatitis following parotitis in a boy aged 4 years, 1 of severe pancreatitis following scarlet fever in a girl aged 7 years and a third case due to parotitis in a boy 4½ years of age who died. Pancreatitis, contrary to the general belief, is a frequent complication of certain diseases. It may subside without stormy symptoms, and only the diminution of some enzymes, especially of lipase, and the resulting deficiency condition leading to celiac syndrome may point to it. It is important that the condition be diagnosed in its earliest stage, as the process is no longer reversible after it has become chronic. In such cases the patients require large doses of pancreatic extracts or enzyme preparations and an almost fat-free diet. Milk can render good service if gastric lipase is present. Parenteral administration of vitamins A, D and K is of importance.

**Islet Cell Tumor of Pancreas.**—In Sherman's case of spontaneous hypoglycemia due to insular tumor of the pancreas (nesidioblastoma) in a newborn infant twitchings and convulsions were observed twenty-four hours after delivery. There was early a good response to administration of dextrose and injection of epinephrine, with a dextrose tolerance curve demonstrating rapid removal of the circulating glucose. Extrapancreatic causes of hypoglycemia were excluded. The mother was nondiabetic. A clinical diagnosis of hyperinsulinism was made and an exploratory laparotomy was performed. Neither resection nor biopsy of the pancreas was performed by the surgeon because the gland appeared normal in size, contour and consistency. This error has been stressed. The necropsy revealed typical islet cell adenoma, almost microscopic in size, and yet the active hormone secreted by it was either so great in amount or so potent in its effect as to cause a fatal outcome; the supportive treatment kept the patient alive for six and one-half weeks despite the severity of the convulsions. The mother's symptoms, including fatigue, somnolence and excessive sweating during the latter part of gestation, are suggestive of a hypoglycemic effect on the mother by the excessive insulin-secretory activity of the fetal pancreatic adenomatous tissue. Routine determinations of sugar in the blood should be made in the neonatal period and in pregnant women with symptoms suggestive of hypoglycemia in the last trimester.

### American Journal of Public Health, New York

**37**:803-958 (July) 1947

Mouse Protection Tests in Study of Pertussis Vaccine: Comparative Series Using Intracerebral Route for Challenge. P. L. Kendrick, Grace Eldering, M. K. Dixon and J. Misner.—p. 803.
Wartime Army Medical Laboratory Activities. G. J. Dammin.—p. 811.
Common Rat as a Source of Erysipelothrix rhusiopathiae. C. H. Drake and Elizabeth R. Hall.—p. 846.
Health Education in Mexico. M. G. Rivera.—p. 849.
Evaluation of Effectiveness of Astoria Plan for Medical Service in Two New York City Elementary Schools. A. Yankauer Jr.—p. 853.
Rickettsialpox: Newly Recognized Rickettsial Disease: III. Epidemiology. M. Greenberg, O. J. Pellitteri and W. L. Jellison.—p. 860.
Inactivation of Partially Purified Poliomyelitis Virus in Water by Chlorination: II. S. G. Lensen, M. Rhian and M. R. Stebbins.—p. 869.
Regionalism in Relation to Health of the Public. C. W. Strow.—p. 889.
Municipal Public Health Engineering: Data on Current and Proposed Local Sanitation Division: L. M. Board and others.—p. 901.
Newspapers: Public Health Allies. P. F. Ellis.—p. 907.

**37**:959-1088 (Aug.) 1947

Health Councils in Local Communities. B. Marquette.—p. 959.
Need for Systematic Evaluation of Substandard Housing. M. A. Pond.—p. 967.
Microbiology of Spray-dried Whole Egg: II. Incidence and Types of Salmonella. Mathilde Solowey, V. H. McFarlane, E. H. Spaulding and Cecilia Chemerda.—p. 971.
Shellfish: Report of the Committee. M. H. Bidwell and others.—p. 983.
*Cheese and Its Relation to Disease. F. W. Fabian.—p. 987.
Cardiolipin and Purified Lecithin as Reagents in Syphilis Serology. A. Harris and J. F. Mahoney.—p. 997.
Importance of a Standard Code for Tabulating Causes of Illness. S. D. Collins.—p. 1002.
Morbidity Statistics Through Periodic Sample Surveys of Households. T. D. Woolsey.—p. 1007.
Experience with Vaccination Against Influenza in Spring of 1947: Preliminary Report. T. Francis Jr., J. E. Salk and J. J. Quilligan Jr.—p. 1013.
Proposed Statistical Classification of Diseases, Injuries and Causes of Death: Prepared by United States Subcommittee. E. S. Rogers.—p. 1017.
Bacteriologic Procedures in Sanitary Air Analysis. W. F. Wells and others.—p. 1023.
Yellow Fever Vaccination, Simple or Associated with Vaccination Against Smallpox, of Populations of French West Africa by Method of Pasteur Institute of Dakar. M. Peltier.—p. 1026.
Allergy in Brucellosis. A. P. Leon and J. Sosa.—p. 1033.

**Cheese and Its Relation to Disease.**—Fabian states that since 1883 there have been reported in the United States and Canada 59 epidemics with 2,904 cases of disease and 117 deaths in which cheese was the causal factor. There is reason to believe that this represents only a part of the disease caused by cheese. The organisms most commonly associated with cheese-borne infections are members of the Salmonella group such as Salmonella aertrycke, schottmülleri, typhosa, suipestifer, typhimurium and choleraesuis; Staphylococci such as Staphylococcus albus and aureus; Brucella melitensis and Clostridium botulinum. Contrary to the opinion of many cheese makers, pasteurized milk makes a consistently higher scoring and better flavored Cheddar cheese than does raw milk. Cheese made from pasteurized milk can be ripened in about half the time required to ripen that made from raw milk, because it can be held at a

higher temperature. There are seven states and Canada that now require cheese to be made from pasteurized milk or cream or to be held in storage for periods ranging from sixty to one hundred and twenty days in lieu of pasteurization. The sixty day holding period is considered too short, because pathogens may survive this storage period, especially if the cheese is held at low temperatures, 40 to 50 F. (5 to 10 C.). A ninety day holding period is considered preferable and one hundred and twenty days still better. All milk used in making soft cheeses should be required to be pasteurized, because many soft cheeses cannot be held for sixty days without spoilage or deterioration in quality.

## Am. J. Roentgenol. & Rad. Therapy, Springfield, Ill.

**58**:1-128 (July) 1947

Developments in Medical Physics Having Application to Radiation Therapy. H. B. Jones.—p. 1.
*Radioactive Phosphorus as External Therapeutic Agent in Basal Cell Carcinoma, Warts and Hemangioma. B. V. A. Low-Beer.—p. 4.
Deposition of Radioactive Metals in Bone as Potential Health Hazard. D. H. Copp, Dorothy J. Axelrod and J. G. Hamilton.—p. 10.
*Retention of Radioactive Iodine in Thyroid Carcinomas: Histopathologic and Radio-Autographic Studies. L. D. Marinelli, F. W. Foote, R. F. Hill and A. F. Hocker.—p. 17.
Nephrocalcinosis. J. H. Vaughan, M. C. Sosman and T. D. Kinney. —p. 33.
Significance of Indentures in Outlines of Atria of Lateral Ventricles After Air Filling. M. H. Poppel and J. F. Roach.—p. 46.
*Cranial Manifestations of Fibrous Dysplasia of Bone: Relation to Leontiasis Ossea and to Simple Bone Cysts of Vault. F. Windholz.—p. 51.
Pulmonary Emphysema and Tuberculosis: Roentgenologic and Pathologic Study. A. Guggenheim.—p. 64.
Loeffler's Syndrome. A. W. Pearlman.—p. 75.
Roentgenologic Characteristics of Diaphragmatic Hernia. B. R. Kirklin and J. R. Hodgson.—p. 77.
Myelographic Demonstration of Avulsing Injury of the Brachial Plexus. F. Murphey, W. Hartung and J. W. Kirklin.—p. 102.
Physiologic Stasis: Cause of Cholecystographic Error. A. A. Brewer. —p. 106.
Roentgen Appearance of Double Gallbladder Simulated by Gallbladder with Congenitally Folded Fundus: Case Report. R. E. Alexander. —p. 112.

**Radioactive Phosphorus as External Therapeutic Agent.**—Despite the obvious possibilities of using radioactive phosphorus ($P^{32}$) solution for external application to the skin, difficulties were encountered by Low-Beer in developing a technic which would insure exactly reproducible exposures and reactions. After experimentation with absorbent cotton, petrolatum, wool fat, blotting paper, acacia, higher alcohols and other substances, it was found that ordinary thin blotting paper is a most suitable vehicle. Blotting paper of known dimensions soaked in measured amounts of radioactive $Na_2HPO_4$ (sodium phosphate) solution, and dried, can be applied easily to any part of the skin. After preliminary experimental studies, about 400 skin lesions have been treated by the external local application of radioactive phosphorus. The lesions included carcinoma, hyperkeratosis, warts and hemangiomas. Over 90 per cent of the lesions disappeared. The author is aware of the inadequacy of expressing the dose by giving the amount of the radiating source and the time of exposure. At present this seems to be the least confusing and misleading dosage determination. The ultimate aim is to express the dose in some unit which will reveal more about the energy dissipated in the tissues. There is no intention to advance the method described in competition with long-established procedures. The present study has served to emphasize the usefulness of one of the many by-products of the chain-reacting piles established for the production of plutonium and uranium 235.

**Retention of Radioactive Iodine in Thyroid Carcinoma.**—Marinelli and his associates state that tissue sections and radioautographs from 19 cases of thyroid carcinoma have been studied during the past three years at the New York Memorial Hospital. Tracer or therapeutic doses of radioactive iodine are administered to the patient by mouth. Within twenty-four to forty-eight hours the surgical procedure is carried out. Blocks of tissue about 2 to 3 mm. in thickness are fixed in 10 per cent solution of formaldehyde. Wherever possible, blocks of noncancerous thyroid are included. The tissue blocks are dehydrated in dioxane and impregnated with paraffin. Thin sections are cut with a microtome, and these are dried in an oven or over a flame. After the sections are dried the paraffin is removed by passing the sections through several changes of fresh xylene. The exposed surfaces of the deparaffinized sections are then placed directly against the emulsion surface of a photographic plate or roentgen film. Among the 19 cases there were 10 in which the presence of radioactive material was detectable by radioautographic determinations. Five of these were examples of benign metastasizing struma. The remaining 5 had the structure of follicular adenocarcinoma. However, the reporting of positive observations in 10 of 19 cases of thyroid carcinoma is misleading because many of these 19 cases were selected. On the basis of present results and the estimation of the relative frequency of the various types of thyroid carcinomas approximately 15 per cent of thyroid cancers may be expected to accumulate radioactive iodine. Radioautographs do not indicate the exact distribution of radiation in a tumor, because they are obtained from radiation originating in a few microns of tissue and not in a tissue block of thickness comparable to the range of the beta particles. Since the isotopes of radioiodine emit gamma rays, there remains the possibility of administering the isotopes in amounts sufficient to deliver gamma radiation throughout heterogenous tumors. Therapeutic attempts now in progress will provide the answer to this question.

**Cranial Manifestations of Fibrous Dysplasia of Bone.**—Windholz says that numerous contributions to the knowledge of polyostotic fibrous dysplasia have established the fact that the skull is frequently involved in this disorder. Roughly, in 10 cases of monostotic skeletal involvement 1 cranial case has been recorded. In moderate skeletal involvement about half the cases show skull changes. In severe skeletal disease the skull participates constantly. Occasionally the skull exhibits the only manifestations of the disease. Pathologic and roentgenologic evidence of foci of the disease are in limited cranial manifestations—small, simple, cystlike bone blisters in the vault. In more advanced cases localized deformities with translucencies and densities within the deformed areas are observed. In later stages extensive, dense, bony islands and spicules become visible in the expanded parts. In severe involvement the entire vault, the base of the skull and the facial skeleton are deformed. Bone deposits are maximal and are localized mainly at the base of the skull and in the face. Prior to the differentiation of fibrous dysplasia from related conditions, misinterpretations were frequent. They were classified as cranial hyperostosis or, if localization was unilateral, as hemicraniosis, hemihypertrophy, unilateral hyperostosis, unilateral von Recklinghausen's disease, osteitis fibrosa cystica of the skull and the like. Most of the advanced cases have been reported as leontiasis ossea. There are indications that skull specimens known as leontiasis ossea were actually fibrous dysplasia. The basic tissue change is replacement of the diploe by connective structures (visualized roentgenographically as translucencies) in which irregular, poorly or completely ossified, nonlamellated bone tissue may develop (visualized as densities).

## Annals of Otol., Rhin. and Laryngology, St. Louis

**56**:245-510 (June) 1947. **Partial Index**

Tissue Changes in Sinus Membranes After Penicillin Treatment. R. A. Fenton and O. Larsell.—p. 245.
*Tracheotomy in Bulbar Poliomyelitis. R. E. Priest, L. R. Boies and N. F. Goltz.—p. 250.
Hearing Impairment Due to Craniocerebral Trauma. W. E. Grove. —p. 264.
*Statistical Study of Poliomyelitis in Relationship to Tonsillectomy. P. M. Pedersen.—p. 281.
Surgical Treatment of Nasopharyngeal Fibroma. J. M. Brown.—p. 294.
Influence of Constitutional Factors in Otologic Conditions. B. J. McMahon.—p. 298.
Diverticulum of the Esophagus. A. C. Furstenberg.—p. 305.
Endaural Surgery for Chronic Mastoiditis. W. W. Morrison.—p. 317.
*Thyroid and the Nose. A. W. Proetz.—p. 328.
Some Physical Properties of the Conduction Apparatus. H. B. Perlman. —p. 334.
*Present Status of Diphtheria. E. H. Place.—p. 347.
"Ménière's"—A Synonym of Confusion. H. W. Lyman.—p. 352.

**Tracheotomy in Bulbar Poliomyelitis.**—According to Priest and his associates, during the 1946 epidemic of poliomyelitis in Minneapolis 400 cases were diagnosed as the bulbar type. In 75 of these tracheotomy was performed, and 29 patients

survived. At some of the hospitals tracheotomy was done when the following indications existed: respiratory distress as evidenced by recurrent cyanosis, coarse rales in the chest and laryngeal stridor; excitement and unmanageability, causing the patient to resist pharyngeal aspiration; stupor of a degree sufficient to make the patient oblivious of the accumulation of secretion in his airway; inability to cough effectively; pharyngeal pooling of mucus; vocal cord paralysis, or intralaryngeal hypesthesia demonstrable by laryngoscopic examination. Physicians in charge of the adult neurology service came to believe that tracheotomy gave the patient his best chance if it was performed before cyanosis occurred, because cyanosis can only be diagnosed clinically when it is rather far advanced and when anoxia has caused irreversible damage to a central nervous system already damaged by the virus. The authors conclude that tracheotomy improves the chance for survival of properly selected patients, and that tracheotomy used in conjunction with various means for producing artificial respiration will enable some patients who are critically ill with poliomyelitis to survive.

**Poliomyelitis in Relation to Tonsillectomy.**—Pedersen reviews material from the files of the San Francisco City and County Hospital and the Children's Hospital of the same city. All facilities for hospitalization of poliomyelitis patients in the city of San Francisco are in the contagion wards of these two hospitals. The incidence of poliomyelitis to the general population in the epidemic year 1943 was in a ratio of 1 to 1,960, while the incidence of poliomyelitis after tonsillectomy for the same period was in a ratio of 1 to 1,782. The incidence of poliomyelitis following recent tonsillectomy is not greatly out of proportion to the ratio of disease to the general population during an epidemic year. However, there is a higher incidence of bulbar and bulbospinal type poliomyelitis in tonsillectomized patients than in nontonsillectomized patients, the ratio being 2 to 1.

**Thyroid and Nose.**—Proetz states that certain indolent and intractable nasal conditions are peculiar to the type of person regarded as hypothyroid. He concludes from a survey of 84 cases that deficiency of the thyroid hormone may result in two types of changes in the nasal mucosa: (1) red, dry, irritated, "chapped" or desquamative; (2) pale and boggy. Patients deficient in the thyroid hormone may have an increased tendency to nasal infection and nasal allergy, which can be corrected by the administration of thyroid extract alone. Headache and nasal obstruction are prominent symptoms. The basal metabolic rate is helpful but not infallible in distinguishing cases suitable for treatment with thyroid extract.

**Present Status of Diphtheria.**—Place thinks that the present interest in diphtheria is probably due to fear of spread of a new virulent type for which antitoxin is more or less ineffectual and conditioned by a prior idea that diphtheria had been quelled. Neither of these ideas is entirely true. Place cites figures on the diphtheria mortality in Boston, Europe and Great Britain to point out that, although fluctuation of the virulence of diphtheria occurs, it is not associated with the development or introduction of a peculiar, fixed strain. The apparent ineffectuality of antitoxin is more likely to be related to the time of treatment and the speed of the toxin's action. If antitoxin is delayed more than twenty-four hours after the onset of the infection some deaths occur, and the percentage death rate rises rapidly with each day's additional delay. The conception of antitoxic immunity to diphtheria in Schick-negative persons has often been too dogmatic. Immunity is relative, and it is impossible to set the level of immunity that will protect under all conceivable conditions of infection and virulence. Immunization with two doses of alum-precipitated toxoid or aluminum hydrate absorbed toxoid at intervals of three weeks to three months or three doses of soluble toxoid every three to six weeks is satisfactory. Booster or recall doses of toxoid every three to five years are considered desirable although not yet proved essential. Children should be given toxoid or a similar antigen preferably between the sixth and eighth months of age. For treatment, despeciated antitoxin treated chemically and with pepsin-hydrochloric acid or a similar digestant has a great advantage, being low in bulk and largely free from protein reactions as compared to the high percentage of reactions from crude antitoxin. Sulfonamide compounds and penicillin have had no effect on the treatment of diphtheria but are of value in reducing the dangers from secondary infections. Penicillin has proved to be the best therapeutic agent available for the carrier state.

## Bulletin of Johns Hopkins Hospital, Baltimore

**80**:299-376 (June) 1947

*Certain Vascular Effects of Curare in Man: The "Histamine" Reaction. D. Grob, J. L. Lilienthal Jr. and A. M. Harvey.—p. 299.
Physiologic Studies in Congenital Heart Disease: III. Results Obtained in 5 Cases of Eisenmenger's Complex. R. J. Bing, L. D. Vandam and F. D. Gray.—p. 323.
Impact of Modern Psychiatry on Medical Education, Medical Practice, and Hospital Organization. L. S. Kubie.—p. 348.

**Vascular Effects of Curare in Man.**—Grob and his associates found that intracutaneous administration of curare and of *d*-tubocurarine chloride to human subjects produced a local flare and wheal with pseudopods. Intra-arterial administration of the drug produced weakness, discoloration, swelling and wheals of the injected forearm and hand; evidence of local and general vasodilatation, and increased secretion of gastric acid. Intravenous and intramuscular administration produced no evident swelling or wheals and less peripheral vasodilatation and secretion of gastric acid. The intracutaneous and intra-arterial administration of histamine produced vascular effects similar to those of curare. The local and general vascular effects of curare were inhibited by the prior or simultaneous administration of the antihistaminic drug, "pyribenzamine" (tripelennamine hydrochloride). The vascular effects of curare suggests that the intra-arterial administration of this drug causes the release of a histamine-like substance which acts first locally and then systemically. This substance apparently also is released after intracutaneous administration of curare and to a lesser degree after intramuscular and slow intravenous injection. The release of a histamine-like substance following the administration of curare may explain the occurrence during curarization of vascular and other phenomena which resemble the effects of histamine. "Pyribenzamine" may prove to be of value in the prevention and treatment of these histamine-like actions of curare.

## Gastroenterology, Baltimore

**9**:1-117 (July) 1947

Gastroscopy and Lymphoma of Stomach. R. J. F. Renshaw and Francis M. Spencer.—p. 1.
*Hyperventilation Syndrome in Gastroenterology. T. E. McKell and A. J. Sullivan.—p. 6.
Tertiary Gastric Syphilis. W. A. Knight and A. Falk.—p. 17.
*Homologous Serum Hepatitis in a Civilian Hospital. L. T. Rosenthal.—p. 28.
Perforations from Proctoscopy. A. F. R. Andresen.—p. 32.
Carotene and Vitamin A Metabolism in Man: Their Excretion and Plasma Level as Influenced by Orally Administered Mineral Oil and a Hydrophilic Mucilloid. A. E. Mahle and Helen M. Patton.—p. 44.
Nutritional State of Patients with Peptic Ulcer as Measured by Vitamin Levels in Blood and Urine. D. Cayer and S. Cody.—p. 54.
Experimental Studies on Biliary Regurgitation During Cholangiography. H. W. Mixer, L. G. Rigler and M. V. G. Oddone.—p. 64.
Effect in Vivo of Sodium Alkyl Sulfate on Peptic Activity. E. R. Breitweiser.—p. 81.

**Hyperventilation Syndrome in Gastroenterology.**—McKell and Sullivan found that in 500 consecutive ambulatory patients with gastrointestinal complaints hyperventilation was recognized 29 times, an incidence of 5.8 per cent. One of the commonest symptoms of hyperventilation is dizziness. Other common symptoms are air hunger, sensation of tingling or numbness, palpitation and precordial or substernal pain. The most important basis for the production of the syndrome appears to be chronic anxiety. Abdominal symptoms are frequently the mechanism by which attacks are initiated. The attacks often occur so frequently that a conditioned reflex is established, which may be reproduced by any of various stimuli originally present. Recognition and demonstration of the hyperventilation syndrome to the patient are frequently the key to the management of a baffling clinical problem.

**Homologous Serum Hepatitis.**—Rosenthal observed during a ten month period 4 instances of probable homologous serum hepatitis on the gastrointestinal service of the Graduate Hospital of the University of Pennsylvania. Six hundred and ninety-five units of blood and plasma (including pooled plasma obtained from the Office of Civilian Defense) were administered to 98 patients. The incubation period ranged from fifty-six to ninety-three days. Because of the onset of icterus following

the administration of blood and plasma, particularly in the absence of any known exposure to other cases of infectious hepatitis, the jaundice was considered to be due to homologous serum hepatitis. The possibility of the jaundice being due to common infectious hepatitis cannot be excluded. Three patients received blood and plasma; 1 patient received plasma only. No frank jaundice was observed in any patient who had received whole blood exclusively during this period. The symptoms were mild. Therapy consisted in the administration of a high carbohydrate, high protein diet supplemented by the parenteral administration of dextrose and amino acids and the use of vitamin supplements, including vitamin K.

## Hawaii Medical Journal, Honolulu

**6**:393-482 (July-Aug.) 1947

Thirty Years' Experience with Coronary Artery Disease. C. C. Sturgis.—p. 393.
*Asthma in the Newborn, or, "Doctor—is it Thymus?" F. D. Nance.—p. 400.
Rh Factor. A Review. L. E. Mermod.—p. 402.
Echinococcus Cyst of Lung. F. L. Giles.—p. 405.
Hearing Defects in Schools. H. E. Crawford.—p. 410.

**Asthma in the Newborn.**—Nance reports 7 cases, which came under his observation and which illustrate the following points: 1. Asthma in the newborn is not uncommon, but is probably the most frequent cause of a wheeze in these infants. 2. It is almost always dietary in origin. 3. Since the diet at this age is extremely limited, the detection of the offending food is simple. The author concludes that the history that an infant wheezed since birth plus the finding of an expiratory wheeze should suggest a probable diagnosis of asthma due to food allergy. Physicians should be unwilling to accept a diagnosis of thymus enlargement as the cause of noisy respiration in the newborn on the basis of roentgen observations alone.

## Journal of Bone and Joint Surgery, Boston

**29**:553-838 (July) 1947. **Partial Index**

Flexor-Tendon Grafts to the Finger and Thumb. W. C. Graham.—p. 553.
Tendinous Reconstruction of Hand Following Irreparable Injury to Peripheral Nerves and Brachial Plexus. C. A. Luckey and S. R. McPherson.—p. 560.
Reconstruction of Defects of Tibia and Femur with Apposing Massive Grafts from Affected Bone. J. J. Flanagan and H. S. Burem.—p. 587.
Calcified Medullary Defects in Bone. A. B. Ferguson.—p. 598.
*Immobilization with Bone Grafts in Treatment of Tuberculosis of Joints and Pott's Disease. E. Sorrel and Madame Sorrel-Dejerine.—p. 603.
Functional Aspects of Abductor Muscles of Hip. V. T. Inman.—p. 607.
*Use of Homogenous Bone Grafts: Preliminary Report on Bone Bank. L. F. Bush.—p. 620.
Repair of Defects of Radius with Fibular Bone Grafts. R. C. Miller and G. S. Phalen.—p. 629.
Operative Treatment of Paralytic Genu Recurvatum. C. H. Heyman.—p. 644.
*Use of Absorbable Substances to Obliterate Bone Cavities and as Hemostatic Agents in Operative Procedures on Bones and Joints. J. Buchman and J. E. Blair.—p. 650.
Experiences with Epiphyseal Arrest in Correcting Discrepancies in Length of Lower Extremities in Infantile Paralysis: Method of Predicting Effect. W. T. Green and Margaret Anderson.—p. 659.
Posterolateral Approach to Femur. G. H. Marcy.—p. 676.
Arthrodesis of Hip Joint in Degenerative Arthritis: Modified One-Stage Procedure with Internal Fixation. J. A. Dickson and L. J. Willien.—p. 687.
Osteochondritis Dissecans of Talus. R. B. Ray and E. J. Coughlin.—p. 697.
Oblique Subcervical (Reverse Intertrochanteric) Fractures of the Femur. L. T. Wright.—p. 707.
*Arthroplasty of Hip for Congenital Dislocation in Children. P. C. Colonna.—p. 711.
Metacarpal Reconstruction. J. W. Littler.—p. 723.
Primary Arterial Injury Complicating Extremity Fractures. D. W. Hedrick, F. B. Hawkins and C. O. Townley.—p. 738.
Operation for Old Unreduced Bennett's Fracture. J. R. Vasko.—p. 753.

**Bone Grafts in Tuberculosis of Joints and in Pott's Disease.**—Sorrel and Sorrel-Dejerine evaluate the use of bone grafts for immobilization in the treatment of Pott's disease and tuberculosis of the joints on the basis of their experience with bone grafting. They have gained the impression that among adolescents, adults and aged persons immobilization grafts have been of great help in the treatment of tuberculosis of the joints; and that in two of its most frequent and most severe localizations, in the spine and the hip, end results have been greatly improved by bone grafts. Among children the use of grafts has brought only slight modifications in the treatment of Pott's disease and tuberculosis of the joints. However, in the sequelae of hip disease these immobilization grafts have been found to be extremely useful.

**Bone Bank for Homogenous Bone Grafts.**—Macewen reported the first successful transplantation of bone from one person to another in 1878, but the use of homogenous bone transplants has received only casual notice. The fate of homogenous bone transplants was uncertain and the preservation and availability of such tissue has been an obstacle. Bush reviews the literature and reports results of bone homografts in 67 operations. He stresses that homogenous bone may be used as a transplant under the same conditions as, or in conjunction with, autogenous bone. The blood type has no influence on the successful use of homogenous grafts of bone, nor does the Rh factor influence the results. Bone may be stored in sealed containers at from 2 to 5 C. for periods up to three weeks. Bone may be preserved in sealed containers in the deep freezer at approximately —25 C. for an indefinite period. Microscopic studies of bone removed from fused areas in which homogenous bone had been used showed the grafts to be dead but surrounded by connective tissue undergoing metaplasia and new-bone formation. The success of homografts of bone has been shown by clinical results, by direct inspection of the fused area and by roentgenographs. Homografts of bone, available in a bone bank, will eliminate a second operation on a normal ilium or tibia, with its possible complications, and will shorten the time of operation and hospitalization.

**Absorbable Substances to Obliterate Bone Cavities.**—According to Buchman and Blair the treatment of chronic osteomyelitis by saucerization and primary closure of the wound under antibiotic influences has brought with it the problem of control of the hematoma which develops in the resultant bone cavity. The use of intramuscular injections of penicillin before and after the operative procedure and of local applications of penicillin before closure of the operative wound, without drainage, has been found to control infection, provided that the procedure has been sufficiently thorough, until the hematoma becomes adequately organized to resist infection. If the hematoma is too large to be organized rapidly, a sinus results. This reestablishes the cavity and exposes the operative site to reinfection from without, with resultant delay or failure of healing. The authors used absorbable gauze and absorbable gelatin ("gelfoam") in an attempt to fill the bone cavity and to control the continued oozing from the operative site. These substances were left in the wound to be absorbed by the tissues and also served as vehicles for penicillin. In some instances "gelfoam" was used as a partial filler of the cavity in conjunction with thrombin to control the oozing and with penicillin to control the infection. The use of oxidized gauze or absorbable gelatin as a vehicle for thrombin and penicillin in filling dead spaces or bone cavities appeared to be inadvisable because of many complications interfering with the healing of surgical wounds by first intention. The use of oxidized gauze or absorbable gelatin with thrombin as hemostatic agents in the presence of troublesome oozing and bleeding is advisable, and at times invaluable, notwithstanding the fact that the final healing of the wound may be delayed, in a considerable proportion of instances, by temporary partial disruption incidental to the evacuation of collections of blood and serum.

**Arthroplasty for Congenital Dislocation of Hip in Children.**—Colonna reports end results of an arthroplasty procedure devised some years ago for the treatment of congenital dislocation of the hip. From his follow-up study of ten to thirteen years he arrived at the following conclusions: 1. The two stage procedure in the younger age group is permanently effective in providing accurate reduction, stability and an excellent range of mobility. 2. Careful attention to details is essential not only in the first and second stages of the operation but also in the early part of the postoperative period. 3. The results have been better with the unilateral than with the bilateral dislocation. 4. The procedure is not to be employed in children beyond the age of 10 years; the best results have been obtained in children under 8 years of age.

## J. Neuropathology & Exper. Neurology, Baltimore

**6**:217-310 (July) 1947

Cranial Trauma and Extrapyramidal Involvement: Cerebral Changes Simulating Those of Anoxia: Clinicopathologic Report of 3 Cases. N. Malamud and W. Haymaker.—p. 217.
Lesions of White Matter of Central Nervous System. M. Scheinker. —p. 227.
Infantile Cerebral Palsy of Hemiplegic Type: Case with Pyramidal and Somaesthetic Deficit. J. W. Papez and A. R. Vonderahe.—p. 244.
Chronic Lymphocytic Choriomeningitis. A. B. Baker.—p. 253.
*Plasmocytoma of Hypothalamus: Clinical-Pathological Report of a Case. J. D. French.—p. 265.
*Fatal Poisoning by Lead Benzine (Clinico-Pathologic Study). L. Bini and G. Bollea.—p. 271.
*Primary Glioblastoma Multiforme of Cerebellum: Report of a Case. C. B. Powell.—p. 279.
Traumatic Dissecting Aneurysm of Left Internal Carotid Anterior Cerebral and Middle Cerebral Arteries. H. M. Dratz and B. Woodhall. —p. 286.
Sodium Cyanide: Sequence of Changes of Activity Induced at Various Levels of Central Nervous System. A. A. Ward Jr. and M. D. Wheatley.—p. 292.
Mechanism of Cerebral Death with Doses of NaCN from Which the Heart Recovers. M. D. Wheatley.—p. 295.
Rapid Staining Procedures for Paraffin Sections of Formalin Fixed Nervous Tissue. D. E. Fletcher.—p. 299.

**Plasmacytoma of Hypothalamus.**—Plasma cell tumors are usually multiple, occurring in bone. Instances of single plasmacytomas of soft tissue have been reported. Sites most commonly involved are the nasopharynx or conjunctiva. In no instance did the tumor arise primarily in the central nervous system. The case reported by French represents such a primary involvement of the central nervous system, the single lesion being found at necropsy in the hypothalamus. The case was that of a woman aged 42. The microscopic appearance of the hypothalamic mass was quite at variance with that anticipated from gross inspection of the sagittally sectioned brain. The expected glial tumor did not materialize. Infection and hemorrhage clouded the microscopic appearance of the area so that the origin and true nature of the mass was obscured. The neoplastic rather than inflammatory nature of the plasma cell accumulation was indicated by the well localized arrangement of the cells. The site of the tumor was the most unusual aspect of the case. It must be considered as a single extramedullary plasmacytoma and not a metastasis, in view of the absence of other foci.

**Fatal Poisoning by Lead Benzine.**—Bini and Bollea describe microscopic and histochemical observations in 2 cases of fatal poisoning by tetraethyl lead. The question is raised as to whether tetraethyl lead exerts its lethal action on the nervous system through the metal combined with organic radicals or through its ethylic radical alone. The authors consider that their inability to demonstrate lead in the nervous system of their 2 patients in the presence of a clinical and histologic picture reminiscent of alcohol intoxication, suggests that at least in these cases the cause of the toxic action was not lead but the tetraethylic radical.

**Primary Glioblastoma Multiforme of Cerebellum.**—Powell states that cross section of a glioblastoma is characterized on gross inspection by a variegated display of colors; numerous areas of degeneration, hemorrhage and, frequently, small cysts; and tremendous edema and distortion, resulting in flattened and pale, sometimes translucent, convolutions. The aptly descriptive name, glioblastoma multiforme, may be appreciated when the tumor is examined microscopically and the confusing series of cellular forms and appearances are revealed. The multiformity of cell type on one hand and the extensive vascular phenomena and areas of necrosis on the other are perhaps the most typical observations. The author reports a verified instance of this tumor arising as a primary and isolated neoplasm of the cerebellum. Only 3 instances of primary glioblastoma multiforme of the cerebellum of reasonable certainty can be found in the literature. Two additional cases are doubtful, 1 because of an incomplete specimen and 1 because of possible misinterpretation of direct tumor extension into adjacent areas. Seven other cases are included as possible instances, although each is considered improbable. Thus primary glioblastoma multiforme of the cerebellum appears to be a rarity. The significance of the fact that this most commonly observed form of glioma does not appear in the cerebellum is unknown.

## New York State Journal of Medicine, New York

**47**:1535-1630 (July 15) 1947

*SYMPOSIUM ON EASTERN ROCKY MOUNTAIN SPOTTED FEVER*

Introduction. S. Krech.—p. 1579.
Case Reports. H. B. Rubler.—p. 1579.
Clinical Experiences in Eastern Spotted Fever. L. B. Davis.—p. 1581.
Epidemiology of Rocky Mountain Spotted Fever. N. H. Topping. —p. 1585.
Diagnostic Aids in Rocky Mountain Spotted Fever. G. R. Cox.—p. 1587.
Vaccine Prophylaxis of Rocky Mountain Spotted Fever. C. C. Shepard. —p. 1589.
Pathologic Changes in Rocky Mountain Spotted Fever. W. W. Brandes. —p. 1590.
Insect Vectors of Rocky Mountain Spotted Fever on Long Island. J. K. Miller.—p. 1592.
State Science Service and Spotted Fever Problem on Long Island. R. D. Glasgow.—p. 1595.
Public Health Aspects of Rocky Mountain Spotted Fever. A. T. Davis. —p. 1596.
Benadryl: Technic for Its Administration. H. Reinstein and T. H. McGavack.—p. 1601.
Use of Penicillin in Surgical Infections: Note of Warning. J. H. Garlock.—p. 1604.
Use of Fibrin Foam in Gallbladder Fossa Following Cholecystectomy. B. J. Ficarra and J. Lionello.—p. 1606.

## Radiology, Syracuse, N. Y.

**49**:1-130 (July) 1947

Pathology of Rheumatic Diseases. D. M. Angevine.—p. 1.
Roentgen Diagnostic Aspects of Chronic Arthritis and Bursitis. L. W. Paul and W. W. Moir.—p. 6.
*Roentgen Therapy in Arthritis, Bursitis and Allied Conditions. E. A. Pohle and J. A. Morton.—p. 19.
Roentgen Diagnosis of Pigmented Villonodular Synovitis and Synovial Sarcoma of Knee Joint: Preliminary Report. R. W. Lewis.—p. 26.
*Appendical Coproliths: Their Surgical Importance. S. F. Thomas. —p. 39.
Problems in Diagnosis of Cancer of Colon. K. S. Davis and W. H. Daniel.—p. 50.
Effects of Estrogenic Therapy on Osseous Metastases from Carcinoma of Prostate. W. C. MacCarty Jr.—p. 54.
Irradiation of Experimental Cerebral Tumors: I. Experimental Production of Brain Tumors in Mice. II. Observations on Effect of X-Radiation on Experimental Gliomata in Mice. Katharine Tansley and C. W. Wilson.—p. 62.
Osteochondritis Dissecans of Ankle, with Reports of 4 Proved Cases. C. E. Vaughan and J. P. Stapleton. —p. 72.
Rupture of Small Intestine Complicating Injury of Pelvis: Report of 2 Cases with Recovery After Delayed Diagnosis and Operation. D. A. Sampson and H. M. Stauffer.—p. 80.
Adrenal Tumor of Liver in Child: Case Report with Roentgenologic Features. H. Seltz.—p. 86.
Characteristics of X-Ray Films and Screens. R. H. Morgan.—p. 90.
Elastic Ruler for Roentgen Pelvimetry. C. Gianturco.—p. 95.

**Roentgen Therapy in Arthritis and Bursitis.**—Pohle and Morton employed roentgen radiation in the treatment of 100 patients with osteoarthritis and 69 patients with bursitis in the department of radiology, state of Wisconsin General Hospital. Most patients received one series of treatments, but about 40 per cent had two series and a small number three. Satisfactory relief from pain was obtained in approximately 74 patients with osteoarthritis; the corresponding figure for bursitis was 57. No theory as to the mechanism of the therapeutic effect is offered; it may be based on a nonspecific analgesic action of the roentgen rays.

**Appendical Coproliths.**—Thomas reports the occurrence of appendical coproliths in 6 patients between the ages of 6 and 56 years. Hypertrophy of the muscle wall of the appendix was observed in 5 of the cases. This may be the mechanism of the intermittent colic, the history of which can be elicited after the presence of the calculus is discovered. The amount of calcium and the degree of hardness of the calculus depend on the age of the fecalith. One of the four largest coproliths yet reported, 3 by 1.5 cm., is included in this small series. When the diagnosis of "chronic appendicitis" is entertained, a roentgenogram of the abdomen with the patient supine should be made to rule out the possibility of a calcified appendical coprolith. The diagnosis of chronic appendicitis is impossible roentgenographically. It is only inferred that when a clearcut history fits with roentgenographic diagnosis of an appendical coprolith, intervention for chronic, recurring appendicitis will yield benefits.

## FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

### British Journal of Ophthalmology, London

**31**:449-516 (Aug.) 1947

*Effect of Aluminum and Its Alloys on Eye. L. H. Savin.—p. 449.

**Effect of Aluminum and Its Alloys on the Eye.**—Savin reports a case in which a piece of aluminum zinc was observed over a period of three years as it lay on the retina of an only eye. The metal was at first bright and silvery. Later it became coated with a white cover probably of aluminum hydroxide. The fragment shifted twice, each time leaving a retinal imprint, before it eventually disintegrated into white powder. In a second case the metal behaved similarly. Twenty-five implantations of aluminum and aluminum alloy fragments were made into the anterior chambers of the eyes of rabbits and 9 into the vitreous chambers. General effects on the eye included lens opacities, striae, dots, vacuoles and irregular opacities. Inflammatory changes in the uveal tract were frequent. Other changes included fundus pigmentation, localized choroiditis and retinitis proliferans. On the basis of clinical and experimental evidence it is concluded that the eye is by no means inert to aluminum.

### British Medical Journal, London

**2**:83-116 (July 19) 1947

Some Aspects of Human Infertility. A. Sharman.—p. 83.
Lymph-Gland Biopsies for Suspected Bone and Joint Tuberculosis: Analysis of 100 Consecutive Cases. G. P. Arden and J. C. Scott.—p. 87.
*Treatment of Inevitable, Incomplete, and Septic Abortion: Analysis of 600 Consecutive Cases. J. McD. Corston and J. Stallworthy.—p. 89.
Work of a Tuberculosis Contact Clinic for Young Children, 1941-5. F. J. W. Miller.—p. 91.
Rhabdomyosarcoma Causing Acute Retention in Infants. E. Minchin.—p. 94.

**Treatment of Abortion.**—Corston and Stallworthy instituted an interventionist attitude in cases of inevitable and incomplete abortion. After the vulva and vagina had been swabbed, the surgeon examined the pelvis to determine the position of the uterus and the state of the cervix in order to avoid perforation by dilators or forceps. If the canal was patulous and placental tissue was in reach it was removed. If not, the cervix was exposed and an oxytocic drug was injected under vision into the cleaned cervix. Unless it was already patulous the cervical canal was dilated to the size of a no. 14 or 16 Hegar dilator. Sponge forceps were introduced, opened, rotated through 90 degrees, closed and withdrawn. This was repeated until no further pieces of placental tissue were removed. Then the cavity was explored with a flushing curet and packed with a sterile gauze roll, which was removed six hours later. In septic cases this pack was impregnated with sulfathiazole powder. This method has been employed in 600 cases of abortion, in 42 of which there was infection on admission. In the cases with infection chemotherapy was started before the uterus was evacuated. There was 1 death in this series. The authors conclude that surgical evacuation of the uterus, if carefully performed, is safe and efficient. The length of stay in the hospital is reduced by this method. The low mortality is attributed to the fact that a team skilled in handling these cases was responsible for them.

### Lancet, London

**2**:79-118 (July 19) 1947

Education of Psychiatrists. A. Lewis.—p. 79.
*Vagal Resection in Treatment of Duodenal Ulcer. I. M. Orr and H. D. Johnson.—p. 84.
*Clinical Thermometers as Possible Source of Cross Infection in Hospital. J. B. M. Green and J. B. Penfold.—p. 89.
Hormonal Treatment of Deficient Lactation: Results with Crude Anterior Pituitary Extract. Margaret Robinson.—p. 90.
Swallowed Pin Retained in Appendix. J. Scholefield.—p. 92.

**Vagal Resection in Treatment of Duodenal Ulcer.**—According to Orr and Johnson the incidence of chronic and recurrent ulceration is increasing and presents a serious problem. Although 80 per cent of ulcers can be healed medically, 65 per cent of the patients have a recurrence within two years. The risk of complications is considerable, since 1 in 4 or 5 patients have serious hemorrhage or perforation while still young. Gastrojejunostomy is a failure as a routine procedure. It carries a mortality of about 2 per cent and does not cure more than half of the patients. Gastrectomy is more successful if it is sufficiently radical, but it is also more dangerous. The operative mortality may be 5 per cent and the recurrent ulceration rate from 2 to 9 per cent. A further percentage is not freed from symptoms and new symptoms may result from the operation itself. Incomplete vagal resection gives poor results. The insulin test is helpful in differentiating complete from partial vagotomies. The authors have done fifty vagotomies or vagal resections in the last two years without a death. The long term results of vagal resection are not yet known, but little is lost if, on occasion, it fails, for a gastrectomy is still possible. A lasting success by vagal resection is a triumph of physiologic strategy, and failure does not spell disaster.

**Clinical Thermometers as Source of Cross Infection.**—Green and Penfold outline the procedures usually employed in taking temperatures in hospital wards and show that these procedures not only are unsound but may be dangerous. The thermometers remain in the sterilizing fluid only a few seconds between one patient and the next. While some antiseptics are bactericidal in a few seconds, these would almost certainly be harmful to the mucosa of the mouth. The use of inefficient antiseptics gives a false feeling of security. The authors suggest that each patient be supplied with a thermometer which he keeps to himself as long as he stays in the hospital. It can be left by the patient's bed in a small jar containing an antiseptic solution. When the patient leaves the hospital, this thermometer must be properly sterilized before being used again. This can be done by washing the thermometer in running cold water, drying it and placing it long enough in some effective antiseptic.

### Medical Journal of Australia, Sydney

**1**:773-804 (June 28) 1947

Observations on 104 Cases of Anterior Poliomyelitis Treated in South Australia. E. F. West and Lois H. Davison.—p. 773.
*Further Observations on Dental Defects in Infants Subsequent to Maternal Rubella During Pregnancy. M. W. Evans.—p. 780.
Comparison of Ointment "Aerosol 5" with Number 5 Against Lewisite. E. R. Trethewie.—p. 785.

**Dental Defects in Infants After Maternal Rubella.**—Of 67 children born to mothers who had rubella during pregnancy, 30 exhibited congenital dental abnormalities, in 20 cases major in degree. Caries was disregarded in this calculation. If caries and restricted arch formation are taken into account, the abnormalities are detectable in 46 of the children. With the exception of 5, the remainder of the infants show other concongenital malformation. The main abnormalities occurred in the children of mothers who had contracted rubella during the first three months of pregnancy; in the "later pregnancy" group the abnormalities were few in number and minor in degree. The main dental abnormalities comprised retardation of eruption, dental caries and hypoplasia of enamel. Three cases of congenital absence of isolated deciduous teeth and 4 of premature eruption of permanent teeth are recorded.

### Tubercle, London

**28**:107-128 (June) 1947

*Survival of Sputum-Positive Consumptives: Study of 1,192 Cases in a County Borough Between 1914 and 1940. W. H. Tattersall.—p. 107.
Fulminant Tuberculous Septicemia and other Atypical Forms of Abdominal Tuberculosis. E. J. Blair and W. Pagel.—p. 115.

**28**:129-152 (July) 1947

Tuberculosis Among the Gurkhas. J. Aspin.—p. 129.
Management of Tuberculous Empyema. A. J. Coello.—p. 136.
Cavitation in Pulmonary Tuberculosis. R. Grenville-Mathers.—p. 139.
Particular Type of Tuberculous Pulmonary Cavitation Tending to Spontaneous Healing. L. Dunner.—p. 144.

**Survival of Sputum-Positive Consumptives.**—The material reviewed by Tattersall comprises 1,192 patients with positive sputum that were given diagnosis between 1914 and 1940. Five per cent of the patients were lost sight of. No difference in prognosis in respect of age or sex is disclosed for adults, but adolescent males are found to have better prospects of survival than adolescent females. No difference in survival is proved for successive quinquennial periods. In 32 per cent of the standard 1,000 cases patients survive five years. In 22 per cent they survive ten years. After a five year survival there is a 50:50 chance of surviving a further fifteen years. After ten years,

there is a 2:1 chance of surviving a further ten years. Differences in the survival of patients experiencing treatment in sanatoriums and patients not doing so appear to be transient only. The clinical features for patients surviving longest show no consistent resemblance to one another.

## Acta Radiologica, Stockholm

**28**:110-185 (April 30) 1947. **Partial Index**

Radiation Thrombocytopenia. H. Mossberg.—p. 110.
Spontaneous Chronic Intestinal Invagination in Adults. P. B. Hansen.—p. 115.
Hyperostosis Cranii. T. Denstad.—p. 129.
*Changes in the Lungs in 126 Cases of Asbestosis Observed in Finland. C. Wegelius.—p. 139.
*Preoperative Roentgen Treatment in Breast Cancer. S. Kaae.—p. 153.
Further Development of the Theory of Biologic Reactions Caused by Roentgen Rays. J. T. van der Werff.—p. 169.
Diagnosis of Ectopic Pregnancy by Hysterosalpingography. B. Nielsen.—p. 185.

**Changes in the Lungs in Asbestosis.**—Wegelius describes observations on 126 cases of asbestosis among 476 workers of the Finska Mineral Company. The patients presented roentgenologic signs of asbestosis; 94 had a mild form, 23 a moderate form and 9 an advanced form of the disease. The roentgenologic changes in the lung are the most important diagnostic criteria. Various stages of asbestosis can be differentiated roentgenologically. In the classification of his material Wegelius followed Saupe's rather than Shull's method. Uncomplicated cases of pure asbestosis usually corresponded to stages 1 and 2. Moderately severe cases with emphysema and thickening of the pleura and pericardium were extremely common, and the roentgenographic changes were usually those of stages 2 and 3. Cardiac enlargement was less frequent in the author's material than the literature indicates. The rather high percentage of advanced cases (compared with statistics from other countries) is probably due to the fact that this industrial disease has only rather recently been given the attention it deserves. Now that careful supervision is exercised the high figures for more advanced stages will presumably be reduced.

**Preoperative Roentgen Treatment in Cancer of the Breast.**—Kaae evaluates the results obtained at the Radium Center in Copenhagen in 301 cases of cancer of the breast. Treatment by radical surgical intervention either followed or preceded roentgen therapy. The patients were observed for from two to thirteen years, 137 of them five years or more. Wegelius divides the cases into two groups. Stage 1 comprises those in which cancer was present only in the breast, stage 2 those in which the axillary lymph nodes were involved. The method of roentgen treatment varied. Prior to June 1, 1938 a moderate preoperative treatment was given, supplemented by a lesser postoperative radiation; after that time only a strong preoperative roentgen treatment was given. Preoperative irradiation seems to improve the results. The frequency of distant metastases was the same in the preoperatively and the postoperatively irradiated group, whereas the frequency of local recurrence was so much greater in the postoperatively treated patients that it may perhaps explain the better results in the preoperatively treated group.

## Annales Paediatrici, Basel

**168**:289-348 (June) 1947

*Infections with Influenza Bacilli and Penicillin (Meningitis, Empyema, Osteomyelitis). W. Hirsch and E. Nassau.—p. 289.
Erythema Annulare Lehndorff-Leiner Without Other Rheumatic Manifestations. W. Winkler.—p. 303.
Significance of Perforation of Bronchus in Tuberculosis of Endothoracic Lymph Nodes. O. Görgényi-Göttche and D. Kassay.—p. 311.

**Penicillin in Influenzal Meningitis Empyema and Osteomyelitis**—Hirsch and Nassau used penicillin treatment in 3 cases of meningitis, 2 of empyema and 1 of osteomyelitis, all caused by influenza bacilli and all affecting young children. The treatment with penicillin was successful. The authors suggest the following general directives for the treatment of purulent infections caused by strains of influenza bacilli sensitive to penicillin. Whenever suppurating meningitis, pleural empyema or osteomyelitis develops in a young child or nursling, penicillin should at once be given intraspinally or into the pleura or muscle until the type of pathogenic organism and its sensitivity to penicillin has been established. The results of these tests determine whether penicillin therapy should be continued. Hirsch and Nassau found that in empyema and in osteomyelitis treatment with penicillin was adequate, provided it was administered in sufficiently large doses. The combined administration of penicillin and sulfadiazine appears to be the method of choice in treatment of influenzal meningitis.

## Archivio di Antropologia Criminale etc., Turin

**67**:1-138 (Jan.-June) 1947. **Partial Index**

*Acute Barium Poisoning. R. Gilli.—p. 24.

**Acute Barium Poisoning.**—Acute poisoning with barium is rare. One hundred and forty-two cases are reported in the literature. Gilli reports the case of a woman aged 28 who was given erroneously a solution containing 30 Gm. of barium chloride instead of sodium sulfate. The patient took only half of the dose when she manifested symptoms of acute poisoning, abdominal cramps and vomiting followed by paralysis and asphyxia. Lavage of the stomach, hypodermic injection of 1 mg. of atropine sulfate, lobeline and other measures failed. Death occurred within nineteen hours. The author observed at necropsy two lesions of medicolegal value in the anatomicopathologic diagnosis of barium poisoning, namely, lesions of the nerve cells of the brain and brown granulations in the renal tubules, the seat of acute lesions.

## Deutsche medizinische Wochenschrift, Stuttgart

**72**:241-272 (May 16) 1947. **Partial Index**

Symptomatology of So-Called Alimentary Intoxications. H. Kleinschmidt.—p. 241.
Etiology of Epidemic Diarrhea in Summer of 1945. K. Nitsch.—p. 244.
*Macrocytic and Megalocytic Anemia in Hunger Edema. E. Koch and P. Lübbers.—p. 254.
Improved Method of Percutaneous Arteriography. Brobeil.—p. 257.

**Macrocytic and Megalocytic Anemia in Presence of Edema.**—Koch and Lübbers discuss the special forms of anemia that appear in the presence of hunger edema on the basis of observations on 15 cases. The anemias were usually hyperchromic, macrocytic and nonhemolytic (13 cases). In 12 patients the anemia was megalocytic, that is, it resulted from a disturbance in the regeneration of the erythrocytes and was accompanied by increased hemolysis. In both forms Castle's intrinsic factor was demonstrable in the gastric juice, and both forms were characterized by their rapid reaction to liver extracts and autolyzed yeast. The authors think that the etiologic factor is a food deficiency, probably of the vitamin $B_2$ complex.

## Schweizerische Zeitschrift für Tuberkulose, Basel

**4**:197-336 (No. 4) 1947. **Partial Index**

*Tuberculous Endocarditis and Congenital Pulmonary Tuberculosis. M. Aufdermaur.—p. 199.
Morbus Boeck with Transition into Ordinary Tuberculosis. E. Bachmann.—p. 210.
Spontaneous Pneumothorax in Besnier-Boeck-Schaumann's Disease. M. Dressler.—p. 229.
Seasonal Influences on Mortality of Pulmonary Tuberculosis and Several Important Groups of Diseases. A. Esseltier and W. Kalt.—p. 237.
Regression in Roentgenologic Picture of Micronodular Lesions of Lungs. R. Jeanneret and P. Siegrist.—p. 247.
Performance Tests in Evaluation of Patients with Silicosis. F. Lang.—p. 257.
*Sedimentation Rate of Erythrocytes and Tuberculosis. P. M. Steiner.—p. 297.

**Tuberculous Endocarditis and Congenital Pulmonary Tuberculosis.**—Aufdermaur describes the occurrence of late pulmonary primary infection with transition into general miliary tuberculosis and tuberculous endocarditis of the chordae tendineae of the tricuspid valve and tuberculous endometritis in a woman aged 26. Hematogenous tuberculosis developed during pregnancy. The infant died on the twenty-fifth day of life as the result of a disseminated primary tuberculosis of the lungs, which resulted from aspiration of amniotic fluid containing bacilli. The author discusses the pathogenesis of tuberculous endocarditis and thromboarteritis and compares the evolution of primary infection in mother and child.

**Erythrocyte Sedimentation and Tuberculosis.**—Steiner shows that, if the sedimentation speed of the erythrocytes is determined with an exact technic and at carefully chosen times and intervals, the plotted curve of the sedimentation rate permits conclusions with regard to diagnosis and prognosis, and it may be a guide to the proper treatment.

# Book Notices

**Cancer: Diagnosis, Treatment, and Prognosis.** By Lauren V. Ackerman, M.D., Pathologist to the Ellis Fischel State Cancer Hospital, Columbia, Mo., and Juan A. del Regato, M.D., Radiotherapist to the Ellis Fischel State Cancer Hospital. Cloth. Price, $20. Pp. 1115, with 745 illustrations. The C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1947.

The first part (one hundred and twenty-five pages) treats of cancer in general. After the introduction comes an excellent review by M. B. Shimkin of the National Cancer Institute of the methods, results and prospects of experimental cancer research. This is followed by chapters on the pathology of cancer and on its treatment. The physics of radiation, its effects on normal tissues and on cancer, the indications for radiotherapy of cancer—the current methods and the clinical control—are described clearly and constructively. The pathologist is reminded that it is now outside his province to decide on the radiosensitivity of cancer on the basis of microscopic structure. While surgical intervention remains the only hope of cure in many forms of cancer, "the day is past when a surgeon can be considered competent simply because he is technically capable of carrying an operation to completion. The cancer surgeon must be pathologist, amateur physicist (and radiotherapist), physiologist and statistician, as well as surgeon and philosopher." With the necessary changes in the words this statement applies also to the radiotherapeutist. It is noteworthy, too, that by cancer research the authors understand "not only laboratory experimentation, but the clinical study of the disease, the constant improvement of the methods of treatment, and the statistical research which this may imply." The book is dominated by the spirit of an advancing cancerology. The other fifteen chapters, some nine hundred and fifty pages, deal with cancer in the different parts of the body except the central nervous system, beginning with cancer of the skin. The chapter on cancer of the respiratory and upper digestive tracts is the longest; next comes that on the rest of the digestive tract, and then that of the female genital tract. Each chapter and subsection follows the same sequence, namely, anatomy, the incidence of cancer and etiology, pathology, clinical evolution, diagnosis, treatment and prognosis. References to articles quoted in the text are listed at the ends of the chapters. The treatment of present choice is indicated in each case but without bias and without details of interest mainly to the trained specialist. The structure of the cancers is clearly described and well illustrated, the naked-eye appearances abundantly so. The number of pictures of cancer of the skin and the lip could be reduced without any loss of clarification of the text. There are seventy-six informative tabulations of significant cancer data of various kinds. Of much interest are the outline sketches of anatomic relations at cancer sites, and especially of the course and distribution of the lymphatics concerned in the metastasis of cancer. The book is well indexed by authors and by subjects. Throughout the book "cancer" is used freely in place of "malignant disease" or "malignant tumor," but "cancerous" could have been used more often than it is in place of "malignant" in the sense of cancerous. One wonders how it happens that a new word, not in our dictionaries, namely "exophytic," is used to describe certain cancers of the lips and elsewhere. Another apparently new word in cancer lingo is "semimalignant," used in discussing mixed tumors of the salivary gland type. The existence of alveolar carcinoma of the lungs is taken for granted without any reference to the claims of anatomists that there are no cells lining the alveolar walls. But these are not important matters of immediate practical significance. The book gives a good, reliable, comprehensive account of the present knowledge of human cancer as a practical problem. It will be of great help to the clinician and the student. The Ellis K. Fischel State Cancer Hospital at Columbia, Mo., may well rejoice that its rich material has been put to such good use by members of its staff in writing a first class textbook on cancer.

**Lebendige Gewebelehre: Eine Histophysiologie auf neuer Grundlage.** Von Dr. med. et phil. Paul Vonwiller, Assistenzarzt an der kantonalen Heil- und Pflegeanstalt in Rheinau (Kanton Zürich, Schweiz). Paper. Pp. 244, with 26 illustrations. Kommissionsverlag Zollikofer & Co., St. Gallen, 1945.

This monograph was written in Moscow, Russia, in 1938-1939; most of the early work was done with the help of Russian assistants. As the title indicates, the present volume deals with microscopic study of living tissues in contrast to the classical method of fixing, staining and mounting thin sections of dead tissues, to which the author alludes in his introductory chapter. Throughout the monograph the author points out that he and his collaborators studied microscopically only living organs "in vivo et in situ."

The material for study consisted chiefly of anesthetized frogs, rats and rabbits, as well as plants. The method of study with high-powered, specially constructed microscopes allowed even the use of oil immersion lenses on otherwise opaque organs whose blood supply was intact. The details of these instruments as well as the micromanipulators (used over twenty years) will be described in a separate volume.

The organs and tissues chiefly studied "in vivo et in situ" comprise the eye (Gullstrand's slit lamp), skin with its capillaries, lymphatics, thyroid gland, kidney, and, with dyes, the capillary permeability, peripheral nerve and single nerve fiber, the nerve nets of the stomach, the olfactory lobe and nerve, the brain and the movements of the cerebrospinal fluid observed through the covering of the fourth ventricle. Observations of this latter assured him that there occurs a continuous movement of the fluid both cephalad and caudad (a sort of circulation). Injection of dilute methylene blue into the circulation while studying the cells of the thyroid gland revealed only a rather permanent blue coloration of the colloid, whereas the methylene blue in the rest of the tissue of the animal (frog) was rather promptly converted into the leukobase (methylene white).

The book constitutes essentially a résumé of the work on vital microscopy done over the past twenty years by the author and pupils (62 references). Dr. Knisely's work is only casually mentioned twice (pp. 31 and 162) and Markee's work not at all. Neither does the bibliography contain a reference to either of these two American investigators, who have worked in this field for about an equally long period of time.

For much of the data one must refer to the author's original scientific contributions. It would appear that in its present state of development the research referred to in this book will be of interest solely to the anatomist, physiologist and pathologist, even though the author considers the material easily adaptable to clinical studies.

**Tuberculosis Hospital Planning and Construction.** By J. Bruno Basil. American Trudeau Society, Medical Section. Written under direction of Committee on Sanatorium Planning and Construction, American Trudeau Society. Paper. Price, $1. Pp. 81. National Tuberculosis Association, 1790 Broadway, New York 19, 1946.

In 1943 a Committee on Sanatorium Planning and Construction was formed by the Medical Section of the National Tuberculosis Association to rewrite the Manual on Sanatorium Planning originally prepared in 1929 and revised in 1939. The first phase of the committee's work was concerned with the collection of information on important trends and changes in sanatorium planning that have occurred in recent years in accordance with modern developments in the treatment and care of tuberculosis. This study led to the development of architectural plans for a 200 bed tuberculosis hospital as well as the publication of the present brochure, a correlative volume on tuberculosis hospital planning and construction. The new edition gives information on practically all phases of sanatorium planning, including the development of individual services and departments. It considers the factors involved in the organization of a hospital program, the selection of an appropriate site, the planning of administrative and general services, x-ray and laboratory facilities, medical and surgical needs, types of accommodations, outpatient requirements, dietary department,

recreation and rehabilitation, auxiliary facilities, storage, housekeeping, laundry, mechanical services and power, electrical communications and fixtures, quarters for personnel and landscaping of hospital grounds. This book, representing as it does a careful study and analysis of the needs of sanatorium services, will be welcomed by medical and administrative personnel, boards of trustees, architects and all others directly concerned in the planning and organization of hospital facilities essential to the modern care and treatment of tuberculosis.

**Pulmonary Tuberculosis: A Handbook for Students and Practitioners.** By R. Y. Keers, M.D., M.R.C.P., F.R.F.P.S., Medical Director, Red Cross Sanatoria of Scotland, Tor-na-Dee, Milltimber, Aberdeenshire, Scotland, and B. G. Rigden, M.R.C.S., L.R.C.P., First Assistant Medical Officer, Red Cross Sanatoria of Scotland. With a foreward by F. H. Young, O.B.E., M.D., F.R.C.P., Medical Officer in charge of the Tuberculosis Dispensary, St. Bartholomew's Hospital, London. Second edition. Cloth. Price, 17s 6d. Pp. 277, with 124 illustrations. William Wood & Co., Mount Royal & Guilford Aves., Baltimore 2; E. & S. Livingstone, 16-17 Teviot Place, Edinburgh 1, 1946.

Although this is about the same size as the first edition, deletions have been made and replaced by new material. This handbook is intended primarily for students and practitioners of medicine. The first chapter consists of a historical sketch of the development of our knowledge of tuberculosis, followed by a chapter on bacteriology in which the tubercle bacillus is presented with reference to types, staining, culture and inoculation methods. Considerable space is devoted to an excellent presentation of the pathology of tuberculosis. Here all the important steps from the development of the primary lesion to fatal, acute and chronic forms of tuberculosis are presented.

Some controversial points are discussed under the subject of epidemiology and resistance in chapter four, for example the statement that greater resistance is present among those who react to tuberculin than among nonreactors. A number of workers will take issue with this statement and point out that the human body never tolerates tubercle bacilli as well as it does at the time of the initial infection. The statement to the effect that relatively few persons infected with tubercle bacilli contract clinical disease may be challenged by such persons as Bogen, who, in an article on "The Toll of Tuberculous Infection" concluded that as many as 50 per cent of infected persons may at some time have clinical lesions (*Am. Rev. Tuberc.* **42**:253 [Aug.] 1940).

The tuberculosis situation differs considerably from country to country and even in various parts of the same country. For example, under the heading Incidence of Infection attention is called to the high percentage of tuberculin reactors among children of such cities as London and Glasgow. Fifty-eight per cent of children between 10 and 15 years of age are infected in London and 45 per cent in Glasgow. This is in sharp contrast to the findings in cities of the United States, such as New York and Chicago, where the incidence of infection among high school students does not exceed 20 per cent, and in smaller cities from 6 to 15 per cent. As morbidity and mortality rates run parallel but on a lower level than the infection rate, one finds the lower morbidity and mortality in parts of the world where the infection rate is low.

The authors point out that there is no difference in the forms of pulmonary disease caused by the bovine and human types of tubercle bacilli, although the human type is responsible for the great majority of pulmonary lesions. Therefore it is felt that there is no great dissimilarity in the degree of virulence between the bovine and the human types of bacilli for human tissues.

Various diagnostic procedures are presented in a concise and clear manner. The authors state that "it is by virtue of its power in provoking the hypersensitive reaction in the infected body that tuberculin, by demonstrating that primary infection has occurred, is of such great value in diagnosis and in mass investigations." Chapter eight contains an excellent presentation of differential diagnosis. All the modern therapeutic procedures, including the more recent developments in chemotherapy, are presented.

The after-care and rehabilitation of tuberculous patients are given proper consideration. The final chapter consists of a discussion of tuberculosis as a national problem, and some valuable suggestions are offered for its solution.

**1946-1947 The Hospital Purchasing File.** Established 1919 as the Hospital Yearbook by the Modern Hospital Publishing Co., Inc. Twenty-fourth edition. Boards. Various pagination. Purchasing Files, Inc., 919 N. Michigan Ave., Chicago 11, 1946.

This book, which is now in its twenty-fourth edition, continues as an excellent source of information and reference on hospital products and buying. It has an alphabetical list of manufacturers and distributors, a directory of 198 pages on hospital equipment and supplies, and a group of twenty-one manufacturers' catalogues covering administrative, dietary and housekeeping departments, laundry, building construction, maintenance and repair materials, plant operating equipment, professional services and facilities relating to surgery, obstetrics, anesthesiology, radiology, pathology, pharmacy, occupational therapy and physical therapy. Included also are special articles and plans with reference to administrative units, maintenance shops, boiler rooms, surgical units, central supply sections and the hospital pharmacy. The value of the book is further enhanced by an extensive check list of hospital equipment, directories of hospital associations, federal and other agencies serving the hospital and allied fields and the lists and references that have been included in relation to technical schools. As in previous years, this volume provides a vast amount of information of special interest to hospital executives and other personnel concerned in administrative functions of the hospital field.

**Hospitals: Integrated Design.** By Isadore Rosenfield. Progressive Architecture Library. Cloth. Price, $10.75. Pp. 308, with 264 illustrations. Reinhold Publishing Corporation, 330 W. 42d St., New York 18, 1947.

This book is based on lectures on hospital planning given under the joint auspices of the New York chapter of the American Institute of Architects and the Department of Public Works of New York City. It contains nineteen richly illustrated chapters giving a wealth of information on practically all phases of hospital planning and construction. There is an initial discussion of hospital needs as well as the integration of hospital services in a fully coordinated community plan. Then follow the general considerations of location, site, orientation, architectural planning and detailed analyses of individual departments, supplemented by numerous floor plans and other illustrative material. Careful consideration has been given to nursing units, diagnostic and therapeutic facilities, x-ray and laboratory services, surgical, obstetric and pediatric departments, outpatient requirements, administrative units and other service departments. Sections have also been included on hospital construction and costs, daylighting and artificial illumination, housing and training facilities, special hospitals and hospitals of limited size. The author with his wide experience in the field of hospital planning has presented a book that will be welcomed by all who are interested in the future planning and development of hospital facilities and services.

**A Textbook on the Nursing and Diseases of Sick Children for Nurses.** By various authors. Edited by Alan Moncrieff, M.D., F.R.C.P., Nuffield Professor of Child Health, University of London, London. Fourth edition. Cloth. Price, 30s. Pp. 744, with 154 illustrations. H. K. Lewis & Co., Ltd., 136 Gower St., London, W. C. 1, 1947.

The first part of this book discusses the general nursing care of the well and the sick child, together with several chapters devoted to general surgical nursing. The second part consists of a presentation of the diseases of children. One is amazed at the amount of information that has been gathered into this volume. There are no wasted words. Its clarity commends it to the nurse as a textbook during her period of training, and its completeness makes it a valuable work of reference when she has begun active work in her profession.

**Bacteria in Relation to Domestic Science.** By C. E. Dukes, M.D., M.Sc., D.P.H. Cloth. Price, $3.75. Pp. 240, with 10 illustrations. Oxford University Press, 114 5th Ave., New York 11; Amen House, Warwick Sq., London, E. C. 4, 1947.

The author has done a commendable job in presenting bacteriology in an interesting form to the student of domestic science. The activities of bacteria which are related to home life and especially to food are well covered. This book can be recommended for bacteriology courses in domestic science.

# Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

## TREATMENT OF SCARLET FEVER

*To the Editor:*—What is the present day method of treating scarlet fever?

M.D., New York.

ANSWER.—Convalescent scarlet fever serum, scarlet fever antitoxin or penicillin may be used for the treatment of scarlet fever. The sulfonamides are probably not helpful in combating the toxemia of the disease. Nevertheless these drugs are of distinct value when complications develop, although it is doubtful that they prevent complications when used as a prophylactic.

Human convalescent scarlet fever is not plentiful now and therefore often difficult to obtain. Scarlet fever antitoxin may be secured from almost any drug store and is indicated particularly in overcoming the toxemia of scarlet fever but is seldom used to treat complications.

Although there does not seem to be any doubt that penicillin is an efficient remedy in the therapy of scarlet fever, its customary method of administration by intramuscular injection is a disadvantage in adopting it for general usage.

Bed rest for at least one week and an adequate amount of fluids are measures that should not be neglected.

Scarlet fever at the present time is a mild disease in this country.

## LIVER FAILURE

*To the Editor:*—There is a tendency today to relate yellow atrophy of the liver to acute infectious hepatitis. I am referring to acute yellow atrophy attributed to arsphenamine and cinchophen. How does yellow atrophy which is observed now and then in pregnancy fit in this picture?

M.D., Ohio.

ANSWER.—The prevailing opinion regarding yellow atrophy of the liver is that it represents one variety of acute liver failure. From a clinical point of view it is a poor term because fatal acute liver failure may occur without much decrease in the liver size. Acute yellow atrophy may be produced by a massive insult from a single etiologic factor such as the virus of viral hepatitis or some hepatotoxin such as carbon tetrachloride or arsenic or, what is perhaps more common, it may be the result of several etiologic factors having a cumulative effect.

In the case of arsphenamine jaundice there is the toxic effect of arsenic, the frequently present syphilitic hepatitis, and usually a superimposed infection with viral hepatitis. Yellow atrophy from cinchophen is probably due solely to the toxic effect of the drug. It is probable that pregnancy imposes some sort of strain on the liver. This may well be of a nutritional nature caused by a deficiency in methionine and related substances. Decreased intake and increased demand for proteins are often present. Such a liver is more vulnerable to viral hepatitis or other liver trauma and can explain the relatively high mortality reported in pregnancy. In addition, eclampsia may be associated with acute liver failure.

## CONCENTRATION OF SULFONAMIDES IN BLOOD AND URINE

*To the Editor:*—It is often difficult to obtain blood samples by venipuncture from infants and young children for various laboratory determinations. However, urine specimens are readily obtained. Is there a definite correlation between urine and blood sulfonamide levels, and can the latter be calculated from the former, assuming unimpaired renal function?

M.D., New Jersey.

ANSWER.—The discrepancies between the concentrations of sulfonamides in the blood and the urine are sufficiently great to make it an unpractical clinical procedure to ascertain the level of the sulfonamide in the blood by determining the concentration in the urine. Furthermore, the concentration of a sulfonamide in the urine is dependent on the urine volume, and some difficulty is encountered in quantitating the total volume of urine excreted by infants. Then too the proportion of free sulfonamide to acetylated sulfonamide varies from one person to another. A more practical method for determining the blood sulfonamide level in infants and children would be to employ the micromethod, in which only a few drops of blood are necessary.

## RADIUM IN THE NASOPHARYNX

*To the Editor:*—Please give me the present status of the use of radium in the nasopharynx in the treatment of chronic nasal allergy and frequent upper respiratory tract infections complicated by severe deafness. Both of these conditions were present in 2 siblings aged 6 years and 4 years. Both have had complete tonsillectomy and adenoidectomy; but over a one and one-half year period have become progressively worse, particularly as far as their hearing is concerned. Can you suggest any other acceptable form of treatment? It is worthy of note that while there is a strong family history of allergy, there is no history of otosclerosis.

M.D., Phoenix, Ariz.

ANSWER.—The use of radium in the nasopharynx in the treatment of frequent upper respiratory tract infections complicated by severe deafness is a procedure of the greatest value. First suggested and popularized by Samuel J. Crowe and his co-workers at Johns Hopkins Hospital eighteen years ago, the method is now generally used and approved, as attested by a large number of favorable reports in the medical literature.

Since adenoids form an integral part of the mucous membrane of the nasopharynx they cannot be completely removed surgically, and nodules which are left hypertrophy quickly. Because of their location, these lymphoid masses, particularly when swollen as the result of infection, block the eustachian tubes. Changes in the middle ear and deafness follow.

Before one uses radium in the nasopharynx, there should be sufficient indication to warrant the procedure. The nasopharynx should be visualized through the nasopharyngoscope to see if the tubal orifices are encroached on or occluded by lymphoid masses. Examination of the ears should show some discoloration of the tympanic membrane and retraction, which may be confined to Shrapnell's area. As pointed out by Crowe, audiograms in these early cases may show only a loss of hearing for the higher frequencies, but, as the condition progresses, successively lower tones are involved until the conversational range is reached.

Various investigators have noted that some children who were being treated for deafness and who were also asthmatic showed a concomitant improvement in their asthmatic condition during radium therapy. This has been particularly true in cases due to bacterial allergy, while the atopic conditions have been less benefited. There have not been reports as to the effect on children with chronic nasal allergy, though presumably, if this is due to a bacterial allergy and the bacteria are in infected nasopharyngeal lymphoid nodules, improvement might also be expected here.

## HISTOPLASMOSIS

*To the Editor:*—The following information regarding histoplasmosis would be appreciated: 1. Has any drug been found to be of benefit other than symptomatically? 2. If not, what drugs have been found to be of no value? 3. How effective is the skin test in confirming the diagnosis? 4. Where can the antigen be obtained for this test or the serum be sent for testing?

M.D., Michigan.

ANSWER.—1. No drug has been found to be consistently beneficial in the treatment of histoplasmosis. Parsons and Zarafonetis (Histoplasmosis in Man, *Arch. Int. Med.* **75**:1 [Jan.] 1945) cited a report of apparent chemotherapeutic success obtained by the use of neostam (stibamine glucoside) in 1 patient with this disease. Another patient apparently derived benefit from treatment with neostibosan (diethylamine paraaminophenylstibimate) alternated with stilbamidine (4-4 diamidinostilbene). These same compounds, however, have failed to alter the course of the disease in other patients. A somewhat similar situation exists with regard to the sulfonamide compounds. These have been unsucessful in several cases, but A. C. Curtis and E. P. Cawley (article to be published) describe healing of a localized genital lesion following the prolonged use (eighty-seven days) of sulfadiazine 4 Gm. daily.

2. Substances found to be of no value include potassium arsenite, neoarsephenamine, sulfarsphenamine, acetarsone, sodium thiosulfate, iodides, ionized metals, ammonium and potassium taftrate, stibophen, quinine, quinacrine hydrochloride, thymol, bone marrow and pentnucleotide. Several trials of penicillin therapy have also been unsuccessful. Reports concerning the clinical use of streptomycin for histoplasmosis have not yet appeared. Seabury and Artis (*Proc. Soc. Exper. Biol. & Med.* **61**:15 [Jan.] 1946), however, have performed in vitro studies which revealed that high concentrations of this antibiotic did not inhibit the growth of Histoplasma capsulatum organisms.

3. At present the skin test with histoplasmin antigens is of questionable diagnostic value. Several patients with proved histoplasmosis have had negative skin tests. Furthermore, large scale epidemiologic studies such as those of Palmer (*Pub. Health Rep.* **61**:475 [April 5] 1946) have revealed a sur-

prisingly high incidence of positive reactors to histoplasmin. This finding has lessened the possible clinical significance of a positive skin test in a particular individual. In addition it should be recognized that histoplasmin antigens have not been standardized, that the relative value of antigens prepared from the yeast phase and from the mycelial phase of H. capsulatum is unknown and that the significance of cross reactions obtained with other mycotic infections has not been defined. Much work remains to be done before the skin test can be properly evaluated either as an adjunct for epidemiologic surveys or as an ancillary aid in the clinical diagnosis of histoplasmosis.

4. Histoplasmin antigen is not commercially available at present. U. S. Public Health Service workers are actively engaged in histoplasmosis research and may be able to supply the desired antigen. It is suggested that a request be addressed to Dr. Michael L. Furcolow, Field Studies Section, Tuberculosis Control Division at the University of Kansas Hospital, Kansas City, Kansas.

Satisfactory serologic tests for histoplasmosis have not yet been devised.

## STATE MEDICINE, SOCIALIZED MEDICINE AND PUBLIC HEALTH

*To the Editor:*—What is the definition of state medicine?

Scott D. Gleeten, M.D., Monrovia, Calif.

ANSWER.—The terms "state medicine," "socialized medicine," "public health" and "sickness insurance" are often used interchangeably. Actually there are distinctions which should be kept in mind.

Socialized medicine is an all inclusive term and connotes a form of medical practice in which the method of distributing medical care is made subject to the uses or influences of groups of persons, the community or the state.

State medicine is a form of socialized medicine in which the state attempts to provide medical services directly to the general population from funds raised by taxation. The end result is that physicians become employees of the state, with medical practice subject to the directives of a third party. Any form of state medicine necessarily embodies the use of compulsion.

Public health is a form of socialized medicine concerned with special groups and special activities for the protection of the health of the people as a whole.

Sickness insurance is a form of socialized medicine, either voluntary or compulsory, concerned only with spreading the cost of medical care.

## ECZEMA WITH MONILIA ALBICANS

*To the Editor:*—What is the best treatment for eczema (chronic and subacute) which is caused by Monilia albicans? It appears in the spring and in the fall and covers the hands and feet. What, if anything, can be done to prevent its becoming active during the times when it is quiescent? What is the best treatment if it appears in the mouth?

Kamal Zody, M.D., Tripoli, Lebanon, Syria.

ANSWER.—The meager description of the condition makes it impossible to arrive at a diagnosis. Monilia albicans is an invader of moist warm areas and therefore produces intertrigo in the large and small folds of the body. For the same reason it is most active in hot humid midsummer weather rather than in the spring and fall. The organism is the most resistant of all the fungi to the fungistatic and fungicidal chemicals which are usually cutaneous irritants and which should be used with great care. Mention is not made as to whether Monilia albicans was found on culture of the tissue. Potassium permanganate soaks in 1:4,000 solution and gentian violet in 3 per cent aqueous solution would be safe and probably fairly effective treatment.

A recurrent semiannular eruption on the hands and feet would suggest a seasonal contact dermatitis or a toxic eruption.

## COLORED RINGS IN TESTS FOR URINARY ALBUMIN

*To the Editor:*—I use Robert's reagent in testing for albumin in the urine. The reagent is composed of chemically pure nitric acid 1 part and saturated solution of magnesium sulfate 5 parts. Frequently in making ring tests which are negative for albumin there appears a ring of crimson-violet (as nearly as I can describe it). I have been unable to determine what substance or substances produce this color show and would appreciate it if you could enligthen me.

Seth W. Ellis, M.D., Anderson, Ind.

ANSWER.—Colored rings near the junction of the fluids may be produced by iodides, urinary pigments, bile or indican, according to Todd and Sanford (Clinical Diagnosis by Laboratory Methods: A Working Manual of Clinical Pathology, ed. 10, Philadelphia, W. B. Saunders Company, 1943, p. 92).

## REFRACTORY ECZEMA IN YOUNG WOMAN

*To the Editor:*—A married woman aged 34 developed an eczematous eruption on the hands during adolescence which has been with her most of the time since. It was treated as an eczema with varying degrees of success, but she was rarely free from discomfort until during her first pregnancy, when the eruption disappeared spontaneously and she was free from it till some months advanced in lactation. This occurred during each of her three pregnancies. Each time the relief was shorter after confinement. During the years before marriage there had been plenty of evidence that the condition was affected by diet and she was restricted after taking tests and experimentation with diets almost to the point of starvation. During the periods of pregnancy she could eat freely and without any restriction whatever. Between the second and third pregnancies antuitrin-S was found to give nearly complete relief for over two years. It was used steadily a short time and then just before menstruation. The beneficial effect of the antuitrin seems to have worn off, and now with the last baby eight months old and menstruation not well established she is having continuous misery. A diagnosis of fungous disease was considered, but treatment directed to that has not helped. Lymphangitis with swollen arms and tender axillary glands have occurred twice.

M.D., Montana.

ANSWER.—The relationship between eczematoid dermatitis and the sex hormones is quite vague. The condition may clear up or get worse during pregnancy. Often it becomes aggravated in the premenstrual phase. There is little scientific evidence which would indicate that the ovarian hormones themselves have any direct action in producing a dermatitis, although it is known that there may be an effect on skin at the times when the estrogenic titer of the tissues is elevated. This may account for certain cases of premenstrual edema, premenstrual acne, pigmentations of the skin during pregnancy, pigmentation of the nipples with maturity and certain other uncommon dermatologic lesions of various types associated with pregnancy. A deficiency of estrogens either at the menstrual period, at which it is temporary, or a constant one at the menopause will result in an increased capillary fragility with a tendency to purpura.

There is the likelihood that the eczema in this patient is of neurogenic origin, although some evidence seems to indicate a possibility of an allergic basis. There does seem to be a typical pattern in this case often seen with psychogenic disorders, relief being obtained with a number of different procedures temporarily but becoming ineffective on repetition of therapy. Relief is obtained, then, through the power of suggestion. It is possible that during pregnancy the patient felt free of responsibility and received more attention, so that some of the nervous tension contributing to the severity of the dermatitis was removed. It is significant that the relief from the dermatitis was shorter after each of three pregnancies, as her return to active duties involved more and more responsibilities.

It is suggested, therefore, that the psychic factors be analyzed to determine whether or not they may play a major role. Treatment would then be based on the results obtained following investigation into this aspect of the patient's condition. It is expected, however, that certain therapeutic measures will be applied as is usual with such cases, such as refraining from washing with water, the use of synthetic detergents instead of soap, and only the mildest of ointments to eliminate irritations of nonspecific nature.

## ENDOCRINE OR ANDROGEN THERAPY AND ENDOMETRIOSIS

*To the Editor:*—A white woman aged 40 had a hysterectomy and oophorectomy because of a widespread endometriosis with questionable implants on the peritoneum of the intestines. My question is, What is the present consensus on the use of estrogens for menopausal symptoms in this type of case? If estrogens are safe to use is there any particular time element before they are started?

M.D., Indiana.

ANSWER.—Estrogens should not be used in the presence of endometriosis because they may reactivate endometrial tissue which is present and also bring about a return of pain. Faulkner and Riemenschneider (*Am. J. Obst. & Gynec.* **50**:560 [Nov.] 1945) reported a case of severe periodic bleeding from endometriosis of the bowel requiring over seventy partial or whole transfusions. Oophorectomy was finally done in December 1941 and the patient remained well until June 1942, when diethylstilbestrol was administered for menopausal symptoms and severe rectal bleeding recurred.

When women develop menopausal symptoms following an operation for endometriosis they should be given testosterone propionate. Usually a 10 mg. tablet taken by mouth daily will give relief, especially if supplemented by 16 mg. of phenobarbital three times a day for a few days at a time. In many instances phenobarbital alone will relieve menopausal disturbances.